VOLUME 50 NUMBER 6

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PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $10.00

Entered as Second Class Matter Jan. 14, 1925, at the Postoffice at Chicago.
Under the Act of Congress of March 3, 1879

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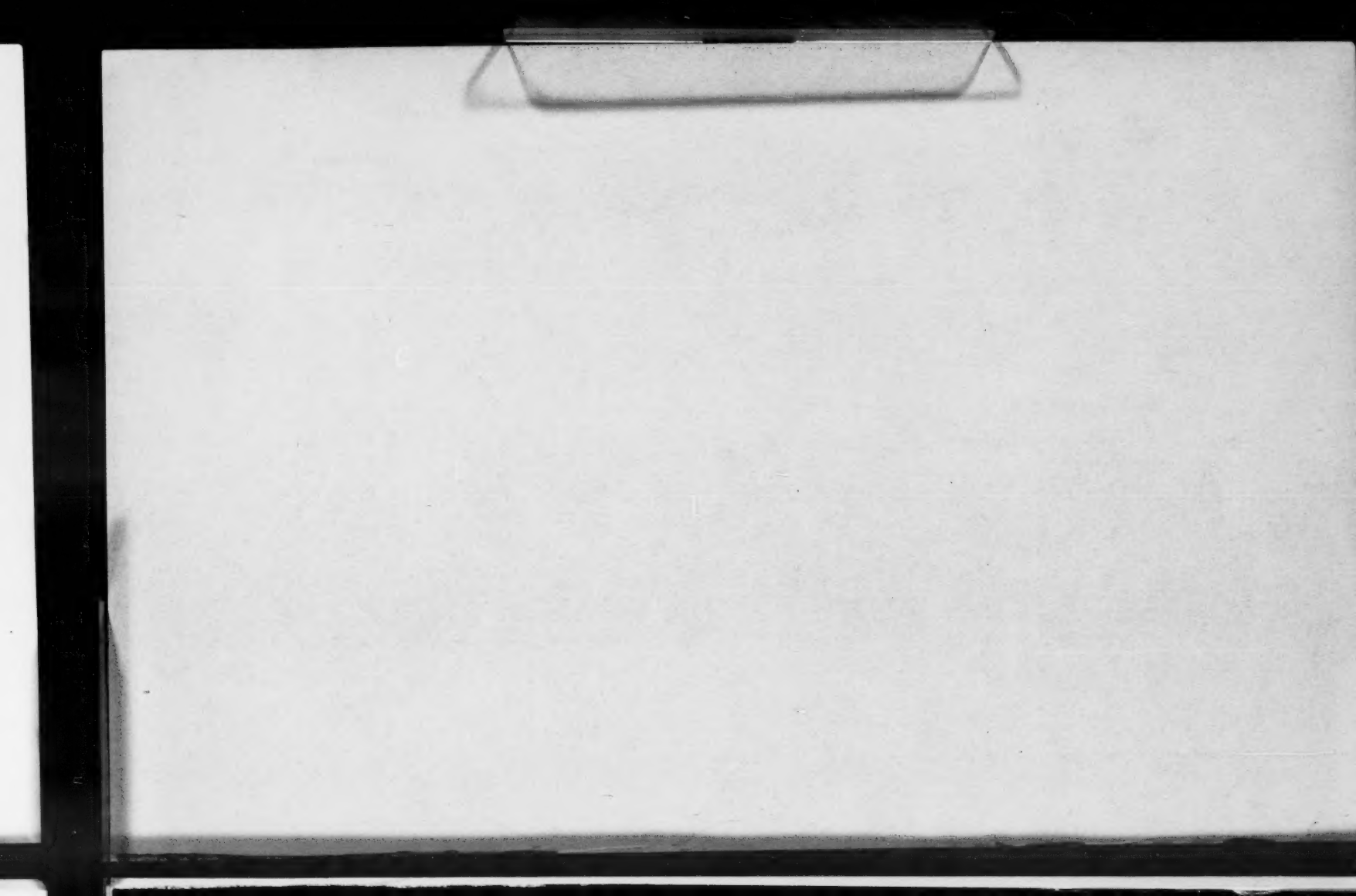

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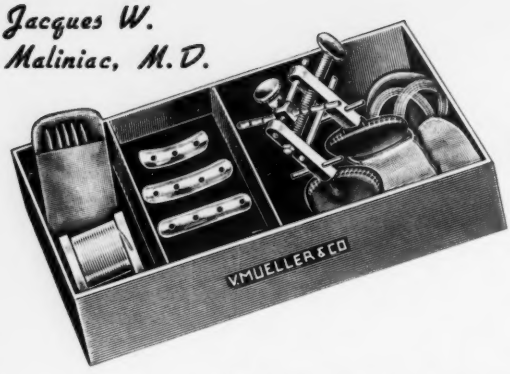

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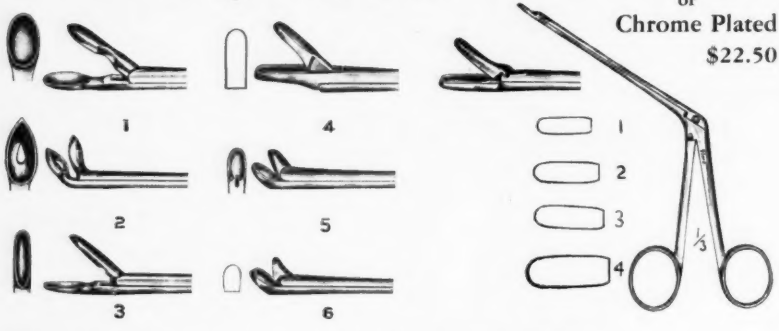

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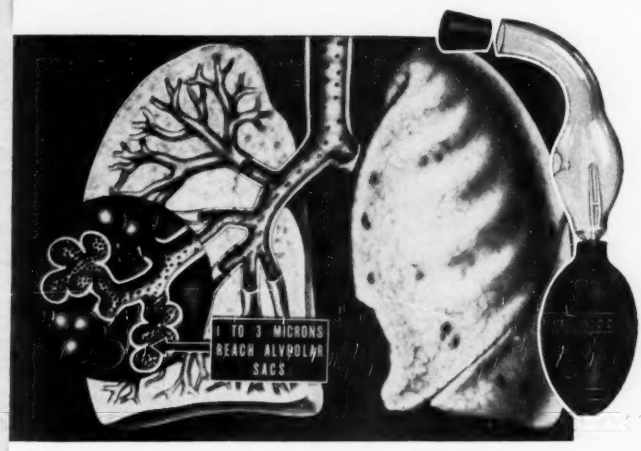

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1. **ABRAMSON, H. A.**: "Principles and Practice of Aerosol Therapy of the Lungs and Bronchi", Annals of Allergy, Vol. 4, November-December, 1946.

2. **BRYSON, V., SANSOME E., AND LASKIN, S.**: "Aerosolization of Penicillin Solutions", Science 100: 33, July 14, 1944.

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VOLUME 50
1949

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ACTIVE IMMUNIZATION AGAINST SECONDARY BACTERIAL INFECTIONS OF THE COMMON COLD

I. Acquired Immunity in Mice Following Oral and Intra-Abdominal Administration of Stock Polyvalent Bacterial Vaccines

JOHN A. KOLMER, M.D.
With the Technical Assistance of Anna M. Rule
PHILADELPHIA

MOST investigators now regard a virus as the cause of the common cold. This primary infection, however, is usually followed within a few days by a secondary bacterial or purulent infection, which not only prolongs the disease but is largely responsible for such complications as sinusitis, pharyngitis, laryngitis, otitis media, tracheobronchitis and pneumonia.

This important secondary infection is due not to any specific bacterium but to one or more of the bacterial species commonly occurring in the upper respiratory tract. In a recent investigation of this phase of the disease, Kolmer, Bondi and Schillinger [1] found that beta hemolytic streptococci of group A, Staphylococcus aureus and various pneumococci (especially Diplococcus pneumoniae of types III, VI, X, XI and XIX) occurred most frequently, although streptococci of the viridans group, gamma streptococci, Staphylococcus albus, Hemophilus influenzae, Klebsiella pneumoniae and organisms of genus Neisseria (especially Neisseria catarrhalis) were found frequently enough to be of additional etiologic significance in some cases.

No attempts have been made up to the present time in active immunization or vaccination of human beings against the virus of the common cold. But, in view of the clinical importance of the secondary bacterial infections of the disease, many investigators have sought to determine whether or not the administration of polyvalent bacterial vaccines possesses prophylactic value against them. My experience has been largely confined to the preparation and administration of

From the Research Institute of Cutaneous Medicine.

This investigation was aided by a grant from The Wm. S. Merrell Company, Cincinnati.

1. Kolmer, J. A.; Bondi, A., Jr., and Schillinger, C.: A Study of the Bacterial Flora of the Nasopharynx in Relation to the Common Cold, Arch. Otolaryng. **47**:571 (May) 1948.

mixed autogenous vaccines by subcutaneous injection. Since 1929 these have been administered during September or October in gradually increasing doses, at weekly intervals, for four weeks in succession, followed by a "booster" dose once a month to May or June.[2] Favorable results have been observed in from 60 to 80 per cent of cases without chronic suppurative sinusitis, consisting in the apparent escape from common colds or the occurrence of but mild attacks limited to a few days without clinically manifest secondary bacterial infections and their complications.

A large and controversial literature, however, has accumulated on the efficacy of stock polyvalent vaccines of desiccated organisms and their soluble products by oral administration in the prophylaxis of the secondary bacterial infections. This involves not only the question of vaccines escaping destruction in the gastrointestinal tract but the absorption of sufficient amounts of the dead organisms or their soluble antigenic substances for the production of effective degrees of immunity.

From the standpoint of oral immunization in the prophylaxis of experimental infections of the lower animals, especially encouraging results have been reported with pneumococci. Thus Ross [3] has shown that rats may be rendered resistant to subcutaneous and intra-abdominal inoculations of 1,000 to 10,000 minimal lethal doses of types I, II and III pneumococci by the oral administration of tissues containing virulent organisms and by vaccines composed of heat-killed, acid-killed, bile-dissolved, desiccated and mechanically disrupted pneumococci and their soluble specific substances. Ross [4] has also found protective antibodies

2. Kolmer, J. A.: Vaccination Against the Common Cold, Arch. Pediat. **46**:41 (Jan.) 1929.

3. Ross, V.: Immunity to Pneumococcus Produced in Rats by Feeding Tissues of Animals Killed by the Same Organism, J. Immunol. **12**:219 (Sept.) 1926; Immunity to Pneumococcus Produced in Rats by Feeding Them the Germ, ibid. **12**:237 (Sept.) 1926; Immunization of Rats Against Pneumococcus by Feeding the Acid-Killed Germs and the Influence of the Age of the Animal Thereon, J. Lab. & Clin. Med. **12**:566 (March) 1927; Oral Immunization Against the Pneumococcus: Use of Bile Salt Dissolved Organisms, etc.; Time of Appearance of Immunity and Dosage, J. Exper. Med. **51**:585 (April) 1930; Oral Immunization Against Pneumococcus Types II and III and the Normal Variation in Resistance to These Types Among Rats, ibid. **54**:875 (Dec.) 1931; The Rôle of the Soluble Specific Substance in Oral Immunization Against Pneumococcus Type I, ibid. **54**:899 (Dec.) 1931; The Rôle of the Soluble Specific Substance in Oral Immunization Against Pneumococcus Types II and III, ibid. **55**:1 (Jan.) 1932.

4. Ross, V.: Protective Antibodies Following Oral Administration of Pneumococcus Type I to Rats, J. Immunol. **27**:249 (Sept.) 1934; Protective Antibodies Following Oral Administration of Pneumococcus Types 2 and 3 to Rats, with Some Data for Types 4, 5 and 6, ibid. **27**:273 (Sept.) 1934.

in the blood of rats following the oral administration of some of these vaccines, especially those for types I, II , III, IV and V pneumococci. Kimura [5] has reported that the oral administration to mice of vaccines of heat-killed pneumococci of type I engendered immunity in some animals, while Kolmer and Amano [6] have observed that the oral administration to rabbits of vaccines prepared of types I, II and III pneumococci and hemolytic streptococci protected some animals against meningitis following intracisternal and intratympanal inoculations with virulent cultures of these organisms. We [7] have also found that the oral administration of vaccines prepared from types I, II and III pneumococci may protect monkeys and rabbits against septicemia and pneumonia following intratracheal inoculations of virulent cultures and, likewise, protect against local pneumococcus infections following intradermal inoculations of virulent cultures.[8]

Much less investigation, however, has been devoted to the oral immunization of the lower animals against other organisms. Winzeler [9] has reported that guinea pigs could be protected against virulent Staph. aureus by the feeding of living organisms less effectively protected by the oral administration of heat-killed vaccines; the oral administration of both living and dead hemolytic streptococci, however, was found much less protective.

PURPOSE OF INVESTIGATION AND METHODS EMPLOYED

In the circumstances, we have thought it advisable to determine whether or not the oral and intra-abdominal administration of polyvalent stock vaccines, proposed for immunization against the secondary bacterial infections of the common cold, is capable of producing resistance or

5. Kimura, R.: Weitere Versuche über aktive Immunisierung per os gegen Pneumokokken, Ztschr. f. Hyg. u. Infektionskr. **107**:390 (April) 1927.

6. Kolmer, J. A., and Amano, K. W.: The Specific Prophylaxis of Pneumococcus and of Streptococcus Meningitis, Arch. Otolaryng. **15**:547 (April) 1932.

7. Kolmer, J. A., and Rule, A. M.: Vaccination of Monkeys Against Pneumococci with Special Reference to Oral Immunization, Proc. Soc. Exper. Biol. & Med. **31**:243 (Nov.) 1933; Oral Immunization of Rabbits Against Pneumococcus Pneumonia and Septicemia, ibid. **30**:107 (Oct.) 1932; Vaccination of Rabbits Against Pneumococci with Special Reference to Oral Immunization, ibid. **31**:245 (Nov.) 1933.

8. Kolmer, J. A., and Rule, A. M.: Vaccination of Rabbits Against Intradermal Pneumococcus Infection, Proc. Soc. Exper. Biol. & Med. **32**:86 (Oct.) 1934.

9. Winzeler, H.: Experimentelle Untersuchungen über orale Immunisierung mit virulenten Staphylokokken und Streptokokken, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:60 (July) 1932.

immunity in mice, even though destruction and absorption of vaccines in the gastrointestinal tract of these animals may be different from that in human beings.

These investigations were conducted over a period of three years. The basic vaccine employed [10] was prepared from D. pneumoniae, hemolytic streptococci (group A), streptococci of the viridans group (respiratory tract), staphylococci, H. influenzae (type A), K. pneumoniae (type A), N. catarrhalis and the concentrated supernatant broth of each bacterium.

Variations of this basic formula were also employed so as to increase the numbers of organisms present and the range of pneumococci and streptococci. Several of these formulas were based on the results of bacteriologic examinations of the nasopharynx by Kolmer, Bondi and Schillinger [1] in cases of the common cold. Placebo tablets were also administered as controls in all experiments.

The oravax® and placebo tablets were ground into very fine powders and 1:100 suspensions in sterile saline solution prepared of each. These suspensions were kept in a refrigerator and thoroughly shaken before administration to fasting mice (18 to 24 Gm.) in doses of 0.5 cc. by stomach once a day for ten days in succession. Mice were also given 0.5 cc. by intra-abdominal injection once a day for ten days in succession.

Protection tests for acquired immunity were conducted fourteen days after the last dose of the vaccines and placebo. The challenging organisms were selected on the basis of their adaptability to mouse protection tests and consisted of hemolytic streptococci (group A), types I, II and III pneumococci and K. pneumoniae (type A) by intra-abdominal inoculation and Staphylococcus aureus by intravenous injection. The virulence of each culture for mice by these routes of administration was determined just before the protection tests were conducted. In the latter each challenging organism was used in approximately 2 minimal lethal doses. Normal control mice were inoculated at the same time in each experiment as culture controls. All inoculated mice were kept under observation for ten days. Cultures of heart blood were made on moribund and most dying mice, and almost all gave positive cultures indicative of septicemic infections.

RESULTS

Since the results observed in the production of immunity by the basic vaccine and by modifications of it were essentially similar, they have been grouped and summarized as shown in the table.

10. Enteric-coated tablets of oravax (improved)® supplied by The Wm. S. Merrell Company, Cincinnati. Each tablet contains:

	Million Cells	Concentrated Supernatant Broth from Million Cells
D. pneumoniae (type I)	5,000	750
D. pneumoniae (type II)	5,000	750
D. pneumoniae (type III)	5,000	750
D. pneumoniae (type VII)	5,000	750
D. pneumoniae (type VIII)	5,000	750
Str. hemolyticus (group A)	10,000	1,500
Str. viridans	5,000	750
H. influenzae (type A)	2,500	375
N. catarrhalis	2,500	None
K. pneumoniae (type A)	5,000	750
Staph. aureus	5,000	750
Staph. albus	5,000	750

It will be observed that about 6.3 per cent of normal control mice inoculated with approximately 2 minimum lethal doses of hemolytic streptococci survived as, likewise, 25 per cent of mice inoculated with Staph. aureus. However, all control mice inoculated with types I, II and III pneumococci and with Kleb. pneumoniae (type A) died. It will also be observed that the oral and intra-abdominal administration of the placebo tablets gave no evidence of engendering immunity against any of the six challenging organisms. Significant degrees of immunity or resistance, however, were observed in mice given the vaccines by oral and intra-abdominal administration, especially against hemolytic streptococci, types I and II pneumococci and Staph. aureus. The same was true, but to a less extent, in the case of pneumococci type III and K. pneumoniae (type A). Although the immunity or resistance against

Acquired Immunity in Mice Following the Oral and Intra-abdominal Administration of Stock Polyvalent Bacterial Vaccines and Placebo

	Vaccines†		Placebo†		
Challenging Organisms*	Oral	Intra-abdominal	Oral	Intra-abdominal	Culture Controls†
Str. hemolyticus (group A).....	28/60 46.6%	34/60 56.6%	0/12 0%	0/12 0%	2/32 6.3%
D. pneumoniae (type I).....	22/60 36.6%	32/60 53.3%	0/12 0%	0/12 0%	0/32 0%
D. pneumoniae (type II).....	8/20 40%	9/20 45%	0/12 0%	0/12 0%	0/24 0%
D. pneumoniae (type III).....	3/12 25%	5/12 41.6%	0/4 0%	0/4 0%	0/16 0%
K. pneumoniae (type A).....	13/52 25%	21/52 40.4%	0/12 0%	0/12 0%	0/32 0%
Staph. aureus.....	9/16 56.3%	12/16 75%	1/8 12.5%	1/8 12.5%	2/8 25%

* Two minimum lethal doses of each culture by intra-abdominal inoculation, except in the case of Staph. aureus, which was injected intravenously.
† Number of surviving mice over total number inoculated, with percentages of survivals.

these organisms resulting from intra-abdominal administration appears to be greater in mice than that following oral administration, an analysis of the data by the chi square method indicates no statistically significant difference.

In the circumstances it appears, therefore, that stock polyvalent vaccines of the desiccated organisms and their soluble products commonly involved in the production of the secondary bacterial infections of the common cold are absorbed from the gastrointestinal tracts of an encouraging percentage of normal adult mice, with the production of immunity or resistance against the virulent organisms employed in this investigation. In this connection it also is to be stated that the 2 minimal lethal doses of each challenging organism employed were highly critical, since the results have been evaluated on the basis of mortality rather than on morbidity rates.

SUMMARY

The results of a study of acquired immunity in mice following the oral and intra-abdominal administration of tablets of stock polyvalent vaccines prepared of the desiccated organisms and their soluble products commonly involved in the etiology of the secondary bacterial infections of the common cold, are presented and discussed.

Active immunity against hemolytic streptococci, types I, II and III pneumococci, K. pneumoniae (type A) and Staph. aureus was produced by the vaccines in a significant number of mice by both routes of administration.

Immunity against the challenging organisms was not produced by the oral and intra-abdominal administration of placebo tablets.

ACTIVE IMMUNIZATION AGAINST SECONDARY BACTERIAL INFECTIONS OF THE COMMON COLD

II. Production of Protective Antibodies in Human Adults by the Oral Administration of Stock Polyvalent Bacterial Vaccines

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With the Technical Assistance of Anna M. Rule
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AS PREVIOUSLY reported,[1] the oral administration to mice of stock polyvalent vaccines prepared from the desiccated organisms and their soluble products commonly involved in the secondary bacterial infections of the common cold has been found effective in the active immunization of some of these animals against virulent hemolytic streptococci, pneumococci of types I, II and III, Klebsiella pneumoniae and Staphylococcus aureus. The investigations of Thomson and Thomson [2] have also shown that such vaccines may be absorbed after oral administration to human beings, in whom agglutinins are then produced. Ross [3] has likewise found that the oral administration of vaccines of pneumococci to human beings not only is well borne but quickly produces immunity, since protective antibodies against the type I pneumococcus

This investigation was aided by a grant from the Wm. S. Merrell Company, Cincinnati, Ohio.

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From the Department of Bacteriology and Immunology of Temple University School of Medicine and the Research Institute of Cutaneous Medicine.

1. Kolmer, J. A.: Active Immunization Against Secondary Bacterial Infections of the Common Cold: I. Acquired Immunity in Mice Following the Oral and Intra-Abdominal Administration of Stock Polyvalent Bacterial Vaccines, Arch. Otolaryng., this issue, p. 687.

2. Thomson, D.: Thomson, R., and Morrison, J. T.: Oral Vaccines and Immunization by Other Unusual Routes, Baltimore, Williams & Wilkins Company, 1948.

3. Ross, V.: Oral Immunization Against the Pneumococcus: Use of Bile Salt Dissolved Organisms, etc.; Time of Appearance of Immunity and Dosage, J. Exper. Med. **51**:585 (April) 1930; Oral Immunization of Humans Against the Pneumococcus, J. Immunol. **27**:307 (Sept.) 1934.

were found in the serums of 75 per cent of subjects and against types II and III pneumococci in the serums of about 60 per cent. Thomson, Thomson and Thomson [4] found that some agglutinins and protective antibodies were also produced in a few volunteers by the oral administration of a phenol-killed vaccine prepared from Hemophilus influenzae grown symbiotically with Anaeromyces bronchitica.

PURPOSE OF INVESTIGATION AND METHODS EMPLOYED

In the circumstances we have thought it advisable to determine whether or not the oral administration of stock polyvalent bacterial vaccines to adult human beings is capable of producing protective antibodies against various virulent challenging organisms in mouse serum protection tests.

These investigations were conducted over a period of three years. The basic vaccine employed [5] was prepared from Diplococcus pneumoniae, hemolytic streptococci of group A, streptococci of the viridans group (respiratory tract), H. influenzae (type A), K. pneumoniae (type A), Neisseria catarrhalis, staphylococci and the concentrated supernatant broth of each bacterium.

Variations of this basic formula were also employed in such a way as to increase the numbers of organisms present and the range of pneumococci and streptococci. Several of these formulas were based on the results of bacteriologic examinations of the nasopharynx by Kolmer, Bondi and Schillinger [6] in cases of the common cold. Placebo tablets were also administered as controls in all experiments.

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4. Thomson, D.; Thomson, R., and Thomson, E. T.: Immunization by the Oral Route in Respiratory Tract Infections, with Special Reference to Influenza, Colds, and Their Complications, Brit. M. J. **1**:258 (Feb. 8) 1936.

5. Enteric-coated tablets of oravax® (improved) were supplied by The Wm. S. Merrell Company, Cincinnati.

	Cells, Millions	Concentrated Supernatant Broth from Million Cells
D. pneumoniae (type I)	5,000	750
D. pneumoniae (type II)	5,000	750
D. pneumoniae (type III)	5,000	750
D. pneumoniae (type VII)	5,000	750
D. pneumoniae (type VIII)	5,000	750
Str. hemolyticus (group A)	10,000	1,500
Str. viridans	5,000	750
H. influenzae (type A)	2,500	375
N. catarrhalis	2,500	None
K. pneumoniae (type A)	5,000	750
Staph. aureus	5,000	750
Staph. albus	5,000	750

6. Kolmer, J. A.; Bondi, A., Jr., and Schillinger, C.: A Study of the Bacterial Flora of the Nasopharynx in Relation to the Common Cold, Arch. Otolaryng. **47**:571 (May) 1948.

Enteric-coated tablets of the vaccines were administered to 116 and the placebo tablets to 35 selected medical students, totaling 151 normal adults. The vaccines were administered according to various dosage scales as follows: (1) 1 tablet a day for seven days in succession, followed by 2 tablets a week for a total of 50 tablets; (2) 1 tablet twice daily for fourteen days in succession, followed by 1 tablet three times a week for a total of 50 tablets; (3) 1 tablet three times a day for seven days in succession, followed by 1 tablet twice weekly for a total of 50 tablets; (4) 2 tablets twice daily for seven days in succession, followed by 4 tablets a week for a total of about 100 tablets; (5) 1 tablet a day for sixty days in succession, followed by 3 tablets a week for a total of about 100 tablets; (6) 1 tablet a day for seven days in succession, followed by 2 tablets per week for a total of about 60 tablets, and (7) 1 tablet a day for a total of about 140 tablets. The placebo tablets were administered according to schedules 1, 4 and 5.

Specimens of blood were collected aseptically from each subject before the administration of the tablets of vaccines and placebo and the serums retained under deep freeze until needed for serum protection tests. Specimens of blood were again collected aseptically two to three weeks after all the oravax* and placebo tablets had been taken and the serums kept under deep freeze for about a month, when the mouse serum protection tests were conducted. On the completion of these tests each subject whose serum showed the presence of protective antibodies against a challenging organism was retested with serum collected before the administration of the tablets for the detection of possible natural antibodies. This policy was adopted for reasons of economy and on the assumption that the serum of a subject showing no protective antibodies after the administration of a vaccine or the placebo was not likely to show their presence in serum collected before administration.

The challenging organisms selected were those best adapted for mouse serum protection tests, embracing virulent beta hemolytic streptococci of group A, pneumococci type I and K. pneumoniae (type A). The virulence of each culture for mice (weighing 18 to 24 Gm.) by intra-abdominal inoculation was determined and each employed in a dose of approximately 2 minimum lethal doses in the serum protection tests. In the latter, each of 4 to 6 mice was given an intra-abdominal injection of a mixture of 0.1 cc. of serum and 0.1 cc. of culture so diluted as to contain approximately 2 minimum lethal doses. In each experiment normal control mice were inoculated intra-abdominally with the same dose of each organism as culture controls. All mice were kept under observation for eight to ten days, when the results were evaluated on the basis of survival over this period. It will be observed, therefore, that

the dose of each challenging organism employed was a critical one, since it was based on mortality rather than on morbidity. Cultures of the heart blood were made on most moribund and dying mice, with positive results in the majority.

RESULTS

On the completion of the mouse serum protection tests, an analysis of the results showed that there were no significant differences in relation to the different formulas of the vaccines or the different dosage schedules employed. In the circumstances and since the purpose of the investigation was to obtain information on the fundamental question of whether or not the polyvalent stock vaccines were absorbed after oral administration, with the production of protective antibodies, the data were grouped for analytic purposes. As previously stated, the serums of those adults

TABLE 1.—*Results of Mouse Protection Tests for Natural and Acquired Antibodies in the Serums of Adults After the Oral Administration of Stock Polyvalent Bacterial Vaccines and Placebo*

Challenging Organisms	Following Administration of Vaccines*	Following Administration of Placebo*	Culture Controls*
Str. hemolyticus (group A)	121/556	12/174	1/78
	21.8%	6.9%	1.3%
Pneumococcus (type I)	98/556	9/174	0/84
	17.6%	5.2%	0%
K. pneumoniae (type A)	187/556	38/174	0/84
	33.6%	21.3%	0%

* Number of surviving mice over total number inoculated, with percentages of survivals.

collected before the administration of the vaccines and placebo were only tested if the serums taken after administration of the tablets showed the presence of antibodies.

An analysis of the results observed on all 151 serums collected after administration of the vaccines and placebo is summarized in table 1, which shows the percentages of mice surviving, because of the presence of both natural and acquired protective antibodies in the serums for hemolytic streptococci, type I pneumococci and K. pneumoniae. This accounts for the fact that some of the serums of subjects who took placebo tablets showed protective antibodies, which were obviously of the natural type, since there was no evidence whatsoever of protective antibodies produced by the oral administration of the placebo.

The results shown in table 2 are also of clinical interest. In this table all serums containing natural protective antibodies were excluded from consideration. In the circumstances it will be observed that none of the serums of 35 subjects taking placebo tablets showed any evidence of protective activity against the three challenging organ-

isms employed, whereas 19.8 per cent showed the presence of protective antibodies against hemolytic streptococci, 25 per cent against type I pneumococci and 19.8 per cent against K. pneumoniae as the result of immunization with the vaccines.

In this connection, however, it was frequently observed that serums collected after the administration of vaccines protected more of the mice employed than serums collected before administration. This suggested

TABLE 2.—*Human Adults Acquiring Protective Antibodies Through the Oral Administration of Stock Polyvalent Bacterial Vaccines and Placebo*

Challenging Organisms	Following Administration of Vaccines*	Following Administration of Placebo*
Str. hemolyticus (group A).....	23/116	0/35
	19.8%	0%
D. pneumoniae (type I).....	29/116	0/35
	25%	0%
K. pneumoniae (type A).....	23/116	0/35
	19.8%	0%

* Number of adults acquiring immunity over total number of adults, with percentages acquiring immunity.

TABLE 3.—*Human Adults Acquiring or Adding to Natural Protective Antibodies Through the Oral Administration of Stock Polyvalent Bacterial Vaccines and Placebo*

Challenging Organisms	Following Administration of Vaccines*	Following Administration of Placebo*
Str. hemolyticus (group A).....	36/116	1/35
	31%	2.8%
Pneumococcus (type I).....	39/116	0/35
	33.6%	0%
K. pneumoniae (group A).....	42/116	3/35
	36.2%	8.6%

* Number of serums showing the presence of antibodies over total number of serums tested, with percentages showing the presence of antibodies.

the presence of acquired protective antibodies in addition to the presence of natural antibodies. Obviously, it is difficult to evaluate such results in terms of acquired antibodies in view of the chances of experimental errors. This seems to be especially true because of the fact that it will be observed in table 3 that the administration of the placebo apparently was followed by an increase of antibodies against hemolytic streptococci in 1 of 35 serums and an increase of antibodies against K. pneumoniae in 3 of thirty-five serums, increases which we attribute to experimental error or too close an analysis of the results of the protection tests with individual serums. With these considerations in mind, however, it will be

observed that approximately 31 per cent of the serums of 116 adults showed acquired protective antibodies in addition to natural antibodies against hemolytic streptococci, 33.6 per cent against type I pneumococci and 36.2 per cent against K. pneumoniae after the administration of the vaccines.

COMMENT

In general terms, the results of this investigation have shown, therefore, that stock polyvalent bacterial vaccines by oral administration may engender the production of demonstrable amounts of protective antibodies in at least some adults, as has been observed in some mice. This affords support for the claims of numerous investigators that the oral administration of such vaccines may be of value in protecting human beings against the secondary bacterial infections of the common cold or shortening their duration and ameliorating their severity.

We have not been interested primarily in this phase of the problem but have merely sought to determine by mouse serum protection tests whether or not there was a basis for the oral administration of stock polyvalent vaccines to human beings for active immunization against these secondary bacterial infections. For this reason we have not attempted to review the large literature on the subject because of the difficulties in drawing reliable conclusions and particularly since factors other than the ingestion of bacterial vaccines may account wholly or partly for escape from common colds. All the results were analyzed statistically by the chi square method. These analyses showed that a significant number of human subjects acquired protective antibodies against hemolytic streptococci, pneumococci of type I and K. pneumoniae after the oral administration of the stock polyvalent bacterial vaccines employed. Whether or not protective antibodies are produced against other pneumococci, streptococci of the viridans group, gamma streptococci, staphylococci, H. influenzae and Neisseria cannot be stated.

SUMMARY

Enteric-coated tablets of stock polyvalent vaccines prepared of the desiccated bacteria and their soluble products commonly involved in the production of the secondary bacterial infections of the common cold were administered orally to 116 adults; placebo tablets were administered to 35 adults as controls.

After administration of the tablets mouse protection tests were conducted with the serums of both groups for antibodies against hemolytic streptococci, type I pneumococci and K. pneumoniae.

The oral administration of the placebo tablets did not produce protective antibodies against any of the three challenging organisms in 35 adults.

The oral administration of tablets of the bacterial vaccines produced protective antibodies against hemolytic streptococci in 19.8 per cent, against type I pneumococci in 25 per cent and against K. pneumoniae in 19.8 per cent of 116 adults when the serums were tested against 2 minimum lethal doses of the respective organisms.

The serums of some adults were found to contain natural protective antibodies against the three challenging organisms. These natural antibodies plus those produced by the vaccines accounted for the combined antibodies against hemolytic streptococci in approximately 31 per cent, against type I pneumococci in approximately 33.6 per cent and against K. pneumoniae in approximately 36.2 per cent of 116 adults.

Under the conditions of these experiments, it appears that the oral administration of tablets prepared of desiccated organisms and their soluble products may produce protective antibodies against hemolytic streptococci, type I pneumococci and K. pneumoniae in a statistically significant number of adults.

SULFAMYLON® AND STREPTOMYCIN IN TREATMENT OF INFECTIONS OF THE EAR

A Preliminary Report

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AND
AUSTIN G. MORRIS, M.D.
ROCHESTER, N. Y.

THE USE of sulfamylon® and streptomycin in local treatment of otitis media with or without acute exacerbation seems to be a valuable addition to the armamentarium of the otolaryngologist. As will be shown, the use of this combination has dramatic results in clearing some types of infections, but in others, especially external otitis, it has no effect.

Sulfamylon,® a sulfanilimide derivative, has a chemical formula of $SO_2NH_2.C_6H_4.CH_2NH_2.HCL$, and a chemical name is 4-(aminomethyl)-benzene sulfonamide hydrochloride. It has a molecular weight of 222.67 and a melting point of 260 to 265 C. (corrected). It is a white crystalline material, soluble in water to 50 Gm. per hundred cubic centimeters at 25 C. and is weakly acid in reaction. Experimentally, this drug is excreted rapidly from the kidneys in three to four hours in the form of a heavy precipitate of a colorless crystalline material. This substance is a deaminated and oxidized product, the chemical name of which is para-carboxybenzene sulfonamide.

Brewer [1] found that in vitro sulfamylon® is highly effective against the anaerobic bacteria Clostridium welchii, Clostridium chauvoei, Clostridium septicum, Clostridium botulinum, Clostridium histolyticum, Clostridium tetani and Clostridium novyi, grown in his thioglycollate sodium medium. Sulfamylon,® on comparison, was found to be bactericidal against these organisms, while sulfathiazole sodium and sulfadiazine sodium not only were found to be nonbactericidal, but were observed to permit some growth of the bacteria in their presence. Quantitatively, sulfamylon® was bactericidal or bacteriostatic to Cl. welchii, Cl. tetani, Cl. histolyticum and Clostridium oedematiens in dilutions up to 1:25,000, while sulfathiazole sodium did not prevent growth of the same bacteria in a 1:100 dilution.

1. Brewer, J. H.: Clear Liquid Mediums for "Aerobic" Cultivation of Anaerobes, J. A. M. A. **115**:598 (Aug. 24) 1940.

Lawrence [2] showed the results of activity against the various anaerobic bacteria in both veal-dextrose serum and Brewer's thioglycollate medium, as contrasted with both sulfathiazole sodium and sulfadiazine sodium (table 1).

Hamre [3] and his associates showed that 2 to 10 Gm. per kilogram of body weight, given perorally to mice, did not produce any evidence of toxic effects. When a 40 per cent solution of sulfamylon® was injected subcutaneously in mice weighing approximately 18 to 20 Gm., no deaths resulted with a dose of less than 6 Gm. per kilogram. The intravenous administration of the solution into mice weighing 20 Gm. at the rate of 0.1 cc. per fifteen seconds showed a LD_{50} of 920 Gm. per kilogram. Experiments with rats showed an oral LD_{50} of 7.4 Gm. per

TABLE 1.[3]—*Highest Dilutions of Sulfamylon,® Sodium Sulfathiazole and Sodium Sulfadiazine Showing Antibacterial Effects Against Various Gram-Positive Cocci**

Organisms	"Sulfamylon"		Sulfathiazole Sodium		Sulfadiazine Sodium	
	Bacteriostatic	Bactericidal	Bacteriostatic	Bactericidal	Bacteriostatic	Bactericidal
Streptococcus haemolyticus.....	1:32,000	1: 8,000	1: 8,000	1:4,000	1: 2,000	<1:1,000
Pneumococcus type I.....	1:32,000	1: 4,000	1:32,000	1:4,000	1: 8,000	1:1,000
Pneumococcus type II.....	1:32,000	1:16,000	1:32,000	1:8,000	1: 4,000	<1:1,000
Pneumococcus type III.....	1:32,000	1: 8,000	1:32,000	1:4,000	1:16,000	<1:1,000
Str. viridans 74.....	1:16,000	1: 400	<1: 100	<1: 100	<1: 100	<1: 100
Str. viridans 1,454.....	1: 8,000	1: 4,000	<1: 100	<1: 100	<1: 100	<1: 100
Str. faecalis 7,080.....	1: 400	<1: 100	<1: 100	<1: 100	<1: 100	<1: 100
Str. faecalis 4,080.....	1: 400	<1: 100	<1: 100	<1: 100	<1: 100	<1: 100

* Figures preceded by < indicate that the highest drug concentration tested proved ineffective.

kilogram. Toxicity experiments were also conducted with rabbits and dogs, and these also showed a high lethal threshold. The effects of the solution on the circulation and respiration of dogs were also studied experimentally. No change except for a slight decrease in blood pressure occurred with subcutaneous injection. Intraperitoneal injection did produce a pronounced drop in blood pressure. The conjunctival mucosa and the mucosa of the urinary bladder were also studied by Hamre [3] for signs of local irritation. Solutions up to 2 per cent were found to have no effect on the conjunctiva, and solutions up to 20 per cent had no effect on the mucosa of the urinary bladder.

Streptomycin is produced by certain strains of the actinomycete Streptomyces griseus. The possible structure of streptomycin has not been definitely proved, but, under acid hydrolysis, streptomycin yields

2. Lawrence, C. A.: J. Bact. **49**:149, 1945.

3. Hamre, D. M., and others: Proc. Soc. Exper. Biol. & Med. **55**:170, 1944.

two moieties, streptidine and a disaccharide-like compound, streptobiosamine. The complete range of antibacterial activity of this drug has not yet been determined,[4] but clinically it has been used with best results in the treatment of infections due to susceptible gram-negative organisms. The dose recommended for topical application is 250 to 500 micrograms per cubic centimeter. If the infecting organisms seem unusually resistant, higher concentrations may be used, as they are easily tolerated by the tissues. The toxicity of streptomycin is very low, and no toxic reactions to its local application have been reported.

In our search for a local therapeutic agent for aural infections, several factors were considered. As necessary attributes, we desired (1) the greatest antibacterial action with the least toxicity to the patient, (2) the widest range of antibacterial action, (3) the easiest and most efficacious physical application of the medicament to the affected part and (4) the greatest chemical stability of the agent to be used.

As determined by Howes,[5] sulfamylon® seemed to be superior to other antibacterial substances tested, while streptomycin was second best. Neither had any toxicity when applied locally; thus fulfilling our first requirement. Sulfamylon,® as previously shown, seemed to have a predilection for bactericidal and bacteriostatic action against gram-positive organisms, while streptomycin tended to exert bactericidal and bacteriostatic action against gram-negative organisms. Thus, the substances fulfilled our second requirement by giving us the greatest antibacterial range possible. In fulfillment of our third requirement, both sulfamylon® and streptomycin were easily soluble, while effective at low concentrations and in solution, and, in fulfillment of our fourth, both were stable indefinitely at room temperature. For these reasons, it was decided to use the combination of sulfamylon,® 5 per cent, and streptomycin, 0.02 per cent,[6] because these substances possessed the best qualities for local action in the treatment of aural infections.

Clinically, Beyer[7] used sulfamylon® and sulfanilamide (1:9) locally on 200 patients as a prophylactic against infection and in treatment of infected wounds and concluded that it was a valuable aid in their treatment. Clark[8] used a 1 per cent sulfamylon® solution as a prophylactic, especially against Bacillus pyocyaneus (Pseudomonas aeruginosa), before operation in his ophthalmic cases. After its use there

4. Clinical use of Streptomycin, Merck and Company, Inc., 1947.

5. Howes, E. L.: Surg., Gynec. & Obst. **83**:1, 1946.

6. This combination was supplied by Winthrop-Stearns, Inc., for clinical research.

7. Beyer, W.: Zentralbl. f. Chir. **68**:1730, 1941; abstracted, War Med. **4**:121, 1943.

8. Clark, W. B.: Local Use of "Sulfamylon" (Para-[Aminomethyl]-Benzene Sulfonamide Hydrochloride), Arch. Ophth. **38**:682 (Nov.) 1947.

were no cases of infection with this organism. There were also no reactions to the drug in his series of 84 cases. Howes [9] conducted studies on the local chemotherapy of wounds, testing streptomycin, sulfamylon,® calcium penicillin, parachlorophenol, tyrothricin and benzalkonium chloride (zephiran chloride®). For local chemotherapy he found that sulfamylon,® 5 per cent, seemed superior to the other antibacterial substances tested, possessed the widest range of antibacterial activity and was relatively nontoxic. It was also found that a mixture of sulfamylon,® 5 per cent, and streptomycin was nontoxic, was relatively stable in the wound and had almost a complete range of antibacterial activity, including the anaerobes of gas bacillus infection. "However, it was unsuccessful in the treatment of open wounds containing slough and sequestrum.[9]" This statement is of importance in dealing with the application of this drug in otolaryngology. Howes,[9] in his experiments with contaminated wounds of rabbits, found that a 5 per cent solution of sulfamylon® combined with a solution of streptomycin (200 units per cubic centimeter) had a high antibacterial action and low toxicity. However, he also found that when the infection had had time to invade the tissues this solution failed to clear it up, or even to speed resolution. In his conclusions, he stated that this failure may have been due to the fact that the solution was prevented from reaching the bacteria, either by the physical barrier of exudate or by the inclusion of the organisms within the dead leukocytes. These bacteria remained susceptible in vitro, however. In his later work,[10] Howes found that prevention of infection could be obtained experimentally as late as forty-eight hours by débridement of crushed tissues and by washing the wound with the sulfamylon® and streptomycin solution. In order to hasten resolution, however, the slough must be liquefied and removed and the bacteria within the leukocytes killed. In December 1947, Fox [11] investigated the use of sulfamylon® in rhinosinusitis. He used it as a nasal spray and as nose drops and in instillations into infected maxillary sinuses. However he found it necessary to use a vasoconstrictor in conjunction with the drug. He used a 1 per cent solution of sulfamylon® against a variety of bacteria and drew the following conclusions: 1. In local treatment of sinusitis sulfamylon® was more effective than penicillin. 2. There is no local or constitutional reaction to the drug. 3. Sulfamylon® is the most valuable of the available chemotherapeutic agents in the local treatment of acute rhinitis and sinusitis. 4. The drug exerted its poorest effect against P. aeruginosa. Our investigation supports the last conclusion.

9. Howes, E. L.: Ann. Surg. **124**:268, 1946.

10. Howes, E. L.: Am. J. Med. **2**:449, 1947.

11. Fox, S. L.: Ann. Otol., Rhin. & Laryng. **56**:946, 1947.

CLINICAL INVESTIGATION

Method and Material.—In the investigation of sulfamylon® and streptomycin therapy, 29 patients were treated. All had aural infections varying from acute external otitis to a chronic otitis media with cholesteatoma. All types of infections were present, and cultures were made wherever possible. The ages ranged from 6 years (acute otitis media) to 67 (chronic otitis media). Because of an insufficient amount of material and in order to control the frequency of administration, the drug was not dispensed to the patient.

The general procedure of treatment of these patients was as follows: After the diagnosis, a culture was obtained when possible. The ear was cleansed thoroughly by dry wiping. We consider this part of the procedure to be very important for the following reasons: Any moisture, either serous or purulent, would prevent the full action of the drug on the infected membranes, both by dilution of the drug and by acting as an actual physical obstruction (Howes [9]). After the removal of the debris, wax, pus or discharge of any nature, the patient was instructed to lie on a couch in the office with the affected ear up. The sulfamylon® was then dropped into the ear and allowed to permeate the structure for fifteen to thirty minutes. A varying amount of the solution was used, depending on the caliber of the external auditory canal and the size of the mastoid cavity. The amount instilled into the ear ranged from 0.25 to 0.50 cc.

In some of our later cases a special needle with a blunt end was devised, so that the solution could be directly instilled into the middle ear through a perforation of any size. This was found to be a valuable adjunct in the treatment. It was reasoned that an extremely small perforation, by reason of pus or granulations in the middle ear, could prevent any of the solution from seeping through the opening. In many ears with chronic otitis media granulations occlude the perforation; these granulations tend to occlude the opening in the drum membrane and prevent contact of the drug with the pathologic middle ear. The granulations were occasionally cauterized with a bead of silver nitrate to check any hemorrhage resulting from the cleansing. After the instillation, the patient was allowed to leave and was requested to have the procedure repeated every other day. Because of transportation and other difficulties, the intervening time, in a number of instances, was of necessity lengthened considerably. The procedure was repeated every other day when possible until a definite reduction in amount of drainage was noted. Then the time interval was lengthened to once a week, once every two weeks or once a month, until complete cessation of drainage was accomplished. The longest period of treatment recorded was five months and the shortest four days, the average length of treatment being about eight weeks. Several patients did not return for treatment, but the results of the last observation has been recorded.

Results.—Prior to the use of sulfamylon® and streptomycin, many of these patients had been under the care of competent otologists, who had used various treatments without results. Sixteen patients with chronic otitis media showed some reduction in the amount of drainage, and in 11 of this number, a dry ear resulted, while the others had a noticeable lessening of the volume of flow. It is interesting to note that in cases in which all, or a large portion, of the drum membrane was absent better and quicker results were obtained. This was, of course, a direct result of the amount of diffusion of the drug over the affected part. In those cases in which only a small perforation was

present, the technical procedure of application of the drug to the middle ear was difficult. Twelve patients had granulations in the middle ear or the external auditory canal, in 7 of these treatment resulted in complete removal and in 4 in a definite reduction in amount; 1 patient did not return for treatment. One patient in this group had a pseudocholesteatoma which had disappeared at the end of treatment. Of 6 patients treated for acute otitis media, 5 had a striking reduction of the disease, while 1 did not return for treatment. All the patients with acute disease were given sulfadiazine or penicillin in conjunction with local therapy. For this reason, no exact evaluation of the efficacy of the treatment could be made, although the ears with the acute infection so treated seemed to dry and clear more rapidly than others with a similar condition in which the local medication was not used. Two of these patients had a perforated drum membrane on their first visit. One patient had a large granulation, which subsided quickly. Six patients had either a simple or a radical mastoidectomy one or more times, the wound continuing to drain after operation until the local sulfamylon® therapy was instituted. Six patients were treated for external otitis, both acute and chronic, and no improvement was noted. In fact, in 3 patients the symptoms and the drainage were aggravated. Several patients had acute external otitis superimposed on chronic otitis media. Before any therapy could reach the middle ear, the acute infection of the external canal had first to be controlled. One patient with acute catarrhal otitis media was treated with no improvement.

Cultures were obtained in a total of 14 cases. In 6 of these cases the cultures yielded entirely, or in part, P. aeruginosa; in 6, Staphylococcus albus; in 3, Staphylococcus aureus; in 1, an undifferentiated streptococcus; in 1, an anaerobic streptococcus; in 1, a streptococcus of the viridans group, and in 1, Aspergillus nigra. In 2 cases of infection with P. aeruginosa a dry ear was obtained. In both cases there were large radical mastoidectomy cavities, through which the medicament could permeate freely; but even then constant treatment for four months was required. In all our other cases of infection with this organism the ear continued to drain, although the amount was slightly decreased. In 1 case of infection with a member of the Staph. albus group combined with P. aeruginosa the ear continued to drain, while in a second case of infection with Staph. albus combined with Staph. aureus the patient did not return for treatment. In 2 of the cases of infection with Staph. aureus a dry ear resulted. Except for the cases of infection with P. aeruginosa and of infection with this organism combined with Staph. aureus, treatment terminated in a dry ear in all cases of otitis media. In 3 cases of external otitis—infection with anaerobic streptococcus, P. aeruginosa and A. nigra, respectively —there was no improvement.

TABLE 2.—*Results of Treatment of Aural Infections with Sulfamylon® and Streptomycin*

Patient	Age, Yr.	Diagnosis	Duration of Drainage	Complications	Condition of Drum Membrane	Culture	Final Results
1	45	Chronic Otitis Media, left	20 yr.	Large granulations and cholesteatoma	Large perforation	80% Staph. albus; 20% hemolytic Staph. aureus	Subsidence of drainage; dissolution of granulations and cholesteatoma
2	42	Chronic Otitis Media, right	4 mo.	Moderate granulations	Large perforation	No culture	Complete subsidence of drainage; dissolution of granulations
3	55	Chronic Otitis Media, right	20 yr.	None	Very small perforation	P. aeruginosa	Very slight decrease in amount of drainage; improvement of physical well-being
4	66	Chronic Otitis Media, right	24 yr.	Large granulations	Large perforation	P. aeruginosa	Slight decrease in amount of drainage
5	33	Chronic Otitis Media, right	19 yr.	Simple mastoidectomy	Very small perforation	Staph. albus; P. aeruginosa	Slight decrease in amount of drainage
6	29	Chronic Otitis Media, right	25 yr.	Large granulations filling radical mastoidectomy cavity	Radical mastoidectomy cavity	P. aeruginosa	Complete subsidence of drainage; dissolution of granulations
7	35	Recurrent Chronic Otitis Media, right	4 days	Large granulations	Large perforation	No culture	Complete subsidence of drainage; dissolution of granulations
8	56	Chronic Otitis Media, right	3 yr.	None	Medium perforation	No culture	Complete subsidence of drainage; healing and closure of right drum membrane
9	20	Chronic Otitis Media, right	10 yr.	None	Medium perforation	Staph. albus	Complete subsidence of drainage
10	21	Chronic Otitis Media, left	2 mo.	Skull fracture through middle ear, with secondary otitis media; granulation	Medium perforation	No culture	Complete subsidence of drainage; dissolution of granulations
11	25	Chronic recurrent Otitis, right	1 yr.	Simple mastoidectomy; large granulations	Large perforation	Hemolytic Staph. aureus	Complete subsidence of drainage; dissolution of granulations
12	23	Chronic Otitis Media, right	17 yr.	Radical mastoidectomy cavity, filled with granulations	Radical mastoidectomy cavity	P. aeruginosa	Complete subsidence of drainage; dissolution of granulations
13	31	Chronic Otitis Media, right	3 yr.	Simple mastoidectomy, small granulations	Small perforation in Shrapnell's area	Staph. albus; Str. viridans	Complete subsidence of drainage
14	26	Recurrent Otitis Media, left	4 days	None	Medium perforation	No culture	Complete subsidence of drainage
15	31	Chronic Otitis Media, right	15 yr.	None	Medium perforation	No culture	Complete subsidence of drainage; subjective improvement in hearing
16	22	Chronic Otitis Media, left	14 yr.	Two simple mastoidectomies	Medium perforation	No culture	Complete subsidence of drainage; closure of perforation in drum membrane
17	30	Acute Otitis Media, right	1 wk.	None	Intact	No culture	Subsidence of drainage; return of drum membrane to normal
18	6	Acute Otitis Media, right	3 days	None	Large granulation	None	Return of drum to normal; disappearance of granulations
19	39	Acute Otitis Media, right	2 wk.	None	Intact	None	Complete subsidence of drainage
20	33	Acute Otitis Media, left	4 days	None	Intact	None	Complete subsidence of drainage
21	67	Acute Otitis Media, right	2 wk.	None	Large perforation	None	Complete subsidence of drainage; closure of perforation
22	20	Acute Otitis Media, right	2 wk.	Medium granulations	Medium perforation	Staph. aureus and Staph. albus	Reduction in amount of drainage; patient did not return for further treatment
23	35	Acute External Otitis, right	1 wk.	None	Perforation, right	No culture	No improvement
24	32	Acute Exacerbation of Chronic External Otitis, Bilateral	10 yr.	None	Intact	Anaerobic streptococcus	No improvement
25	48	Acute External Otitis	1 wk.	None	Intact	P. aeruginosa	No improvement
26	41	Acute External Otitis	2 mo.	None	Small perforation	Staph. albus	No improvement
27	35	Acute External Otitis, right	2 mo.	Small perforation	Small perforation	A. Niger	No improvement
28	52	Acute External Otitis, right	3 days	Granulations in external canal	Intact	Staph. albus	
29	48	Acute Catarrhal Otitis Media, right	None	None	Intact	No culture	No improvement

In order to obtain the best results with sulfamylon® and streptomycin therapy, the following procedures and condition should be fulfilled: (1) thorough cleansing and drying of the area to be treated; (2) application of the solution every day or every other day until drainage has ceased, or at least has been materially reduced; (3) a large perforation of the drum membrane or an open ear cavity; (4) free drainage and liquefaction of secretions; (5) culture.

Data on the entire series of cases, with the final results in each case, are presented in table 2.

CONCLUSIONS

A solution of sulfamylon,® 5 per cent, and streptomycin, 0.02 per cent, is an effective local bactericidal agent in the treatment of chronic otitis media.

No local or systemic reaction to the drugs was noted in this series of cases.

This medication is not effective in the presence of an intact ear drum membrane.

There is no effective antibacterial action on external otitis, either acute or chronic.

There is very little bactericidal action on P. aeruginosa.

The solution of sulfamylon,® 5 per cent, and streptomycin, 0.02 per cent, cannot exert its full bactericidal effect in the presence of pus or debris and is more effective where there is free drainage of the liquefied exudate.

277 Alexander Street.

PREVENTION OF MOTION SICKNESS BY INTRAVENOUS INJECTION OF SODIUM BICARBONATE

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THE TERM "motion sickness" is here meant to include the conditions produced by accelerated motion of trains, ships, planes or other vehicles. Rosenbach called this condition *"Kinetosen,"* and Starkenstein termed it *"Bewegungskrankheit,"* which means sickness caused by undulation. This motion sickness, or "acceleration disease," is produced by rectilinear acceleration acting on the otoliths in the labyrinth.

The experiments made by my associates and myself on animals and man indicate that intravenous injection of sodium bicarbonate dissolves the otoliths and prevents the symptoms usually produced by motion sickness.

These experiments were conducted by exposing rabbits to the up and down motion produced by an apparatus making sixty-three "up and down" trips per minute for a distance of 43 cm. During this process, various changes in the rabbit were recorded. There was a decided increase in respiration and a noticeable inspiratory quickening. Gastric and intestinal action were quickly suppressed and soon ceased. When the rabbit had been exposed to the action fifteen minutes, the following changes in the blood were detected: decrease in lymphocytes, decrease in alkali reserve, increase in sugar, lowered calcium level, increase in sedimentation rate and lowered coagulation time. A fall in rectal temperature was also noted, along with urinary changes showing increased specific gravity, glycosuria, increased creatine and creatinine. In those animals exposed to the movement three hours a day for a total of more than a hundred hours, considerable degeneration appeared in the ganglion cells of the sympathetic nerves at the neck and abdominal cavity but not in the ganglion nodosum of the vagus nerve.

According to the literature, these phenomena are produced by strain on the sympathetic nervous system. To corroborate this, we exposed animals in which the vagus nerve was cut to the same motion. These animals reacted as the animals previously described did. However, when animals that had undergone sympathectomy were exposed to this

Manuscript edited by Joseph Sataloff, M.D., Philadelphia.

up and down motion, the described phenomena were almost completely absent (the sympathetic nerves had been cut at the neck and at the intestine). In the animals that had had a vagotomy there was a decrease in lymphocytes, but when the solar plexus was removed this did not occur. This situation indicates that the changes caused by exposure to the up and down motion are produced by excitement of the sympathetic nerves.

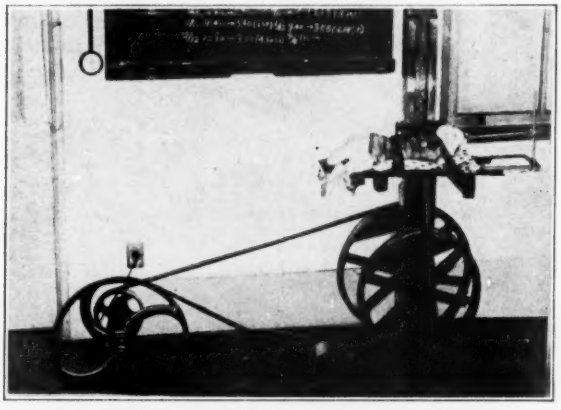

Fig. 1.—Rising and falling apparatus used with rabbit.

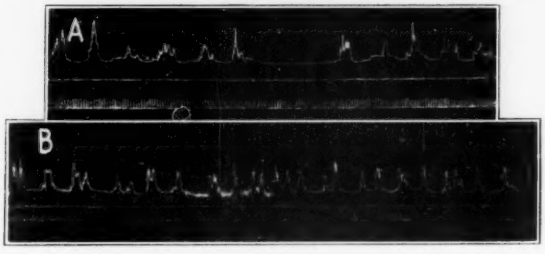

Fig. 2.—Chart of movement of intestine at time of elevation. *A*, animal with vagus nerve cut. Movement of intestine stops while animal is rising and falling. *B*, animal with splanchnic nerve cut. Movement of intestine does not stop while animal is rising and falling.

The experiment was next repeated on animals in which the labyrinths were destroyed. Similar to the sympathectomized animals, these rabbits also revealed no changes in the blood, urine, respiration or intestinal tract. This indicates that the action of the sympathetic nerves induced during this experiment is controlled by the labyrinth.

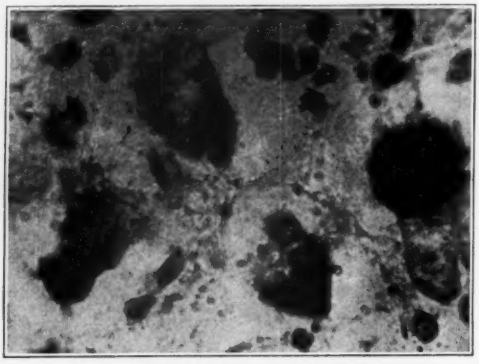

Fig. 3.—Degeneration of cervical ganglion cells.

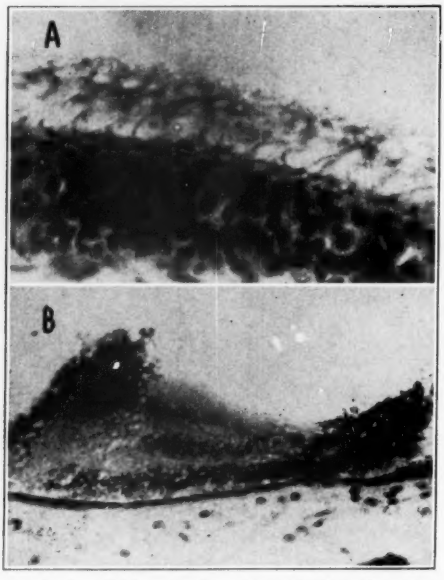

Fig. 4.—Removal of otolithic membrane by subjection of rabbit to the force of centrifugal motion. *A*, macula; *B*, otolithic membrane.

While working in Professor Wittmaack's laboratory in Hamburg, I observed that guinea pigs subjected to centrifugal motion had their otoliths torn off and could not be affected by rectilinear motion. To confirm this result, I centrifuged a number of rabbits in a hare centrifuge and used a force of about 360 g. As was expected, the symptoms and signs of motion sickness did not appear, and histologic sections later

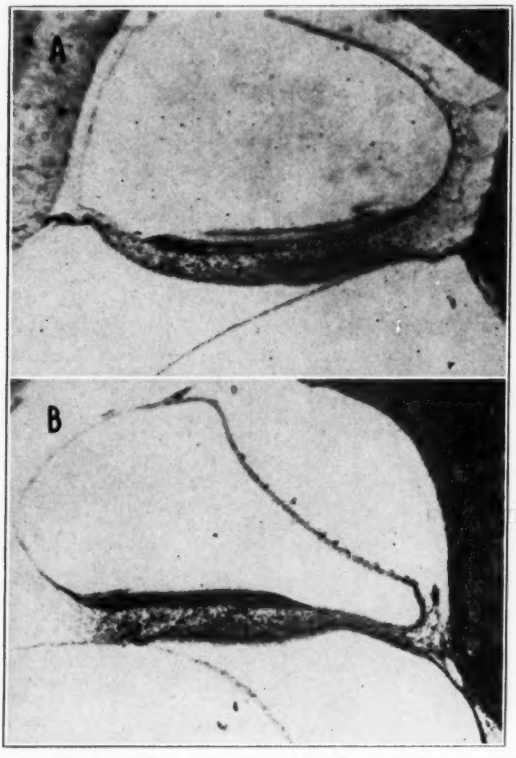

Fig. 5.—*A*, normal rabbit utricle; *B*, utricle after injection of sodium bicarbonate. Low magnification.

showed that the otoliths in these animals had disappeared. As a result of these experiments, I concluded that removal of the otoliths in animals, and perhaps in man, would possibly prevent the condition of motion sickness.

A most interesting observation is that there seems to be no abnormal change in animals deprived of their otoliths; no change could be detected

in their equilibrium, movements or daily routine. According to the hypotheses of Mach, Breuer, and Crum Brown, otoliths are essential to the perception of change in position, and without them, body equilibrium would be difficult to maintain. But no such phenomenon occurred in the experiments. This led me to believe that the removal of otoliths in man would not hinder him in any way and would prevent motion sickness. Since centrifuging a human being was out of the question,

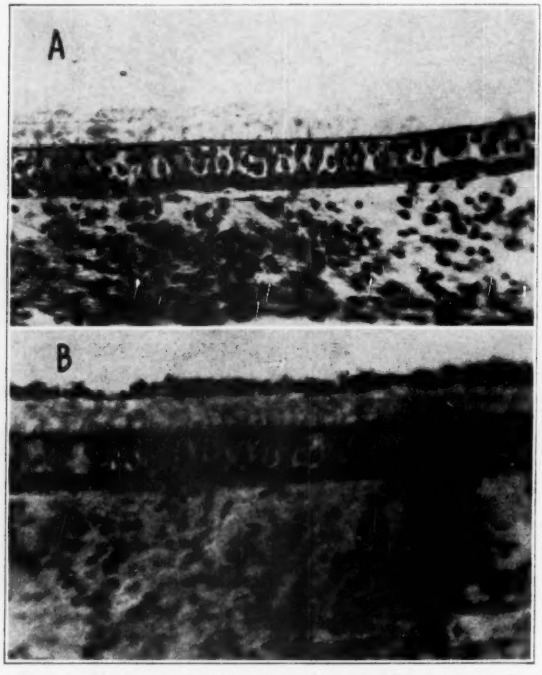

Fig. 6.—High magnification of portions of fields in figure 5.

an approach directed toward chemically dissolving the otoliths in a person was decided on. Observing that the otolithic crystals were formed even better in animals that had received diluted hydrochloric acid intravenously (1 cc. of 0.5 per cent solution once daily), I decided to use sodium bicarbonate. Five cubic centimeters of 5 per cent solution of sodium bicarbonate was injected into the veins of the ears of a number of rabbits. All these animals responded to the up and down motion as if they had been sympathectomized and showed none of the signs of

motion sickness. Histologic examination revealed that the otolithic crystals were gone, with a fine mesh and the glue substance between the former crystals remaining. All these animals responded as if their labyrinths had been destroyed.

Following is an account of the chemical investigation of this phenomenon:

I made an experimental test to see what chemical caused the disappearance of the otolithic crystals. I made an injection of such sub-

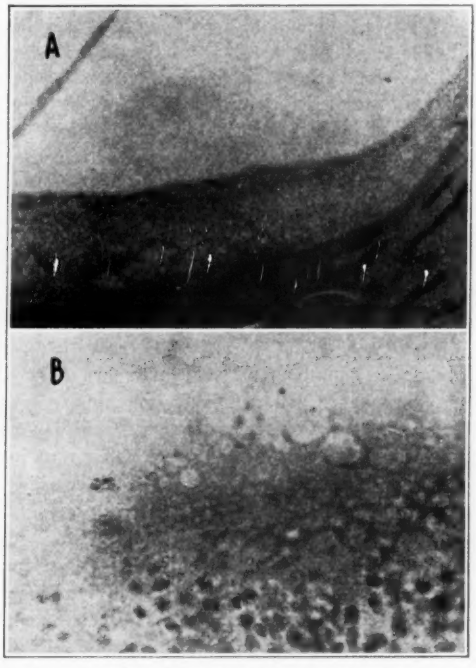

Fig. 7.—Removal of otolithic crystal by intravenous injection of sodium bicarbonate in the case of nasal sarcoma. *A*, low magnification; *B*, higher magnification.

stances as sodium bicarbonate and sodium oxalic acid, but the results showed that the otoliths did not disappear. What makes the otoliths dissolve? It appears that the carbon dioxide generated from sodium bicarbonate works on the solid otolithic crystals of calcium carbonate and produces soluble calcium bicarbonate, the same as in the case of marble becoming dissolved by efflorescence.

To generate carbon dioxide from sodium bicarbonate requires a temperature of 150 C. or higher. This fact coincides with that induced from the animal experimentations. When sodium bicarbonate is sent into the blood of frogs, cold-blooded animals, through their heart, their otolithic crystals do not dissolve. It is also a fact that when carbon dioxide works on the otolithic crystals they do dissolve.

I scratched the otolithic membrane with a sharp spoon by inserting the spoon into the labyrinth of a frog and injected the substance thus taken into water in test tubes. The transparent water became milky. Microscopic examination of a drop of this water revealed innumerable various-sized crystals of the otolith floating on it. I then inserted a pipet into the test tube and blew through it to allow carbon dioxide to work on the liquid. The milky liquid became transparent by degrees. When this practice was continued for thirty minutes or so, the liquid became perfectly transparent, and in microscopic examinations it was difficult to notice any otolithic crystals.

It is inconceivable that sodium bicarbonate injected into a vein will generate carbon dioxide at once and will reach the labyrinth and dissolve the otolithic crystals. It seems more likely that the sodium bicarbonate solution reaches the labyrinth and gets to the cavity below the otolithic membrane; then the work of the carbon dioxide is performed.

APPLICATION OF OBSERVATIONS TO MAN

The commonest symptoms of seasickness are fatigue, depression, dizziness, weakness, facial pallor, difficult breathing, nausea and vomiting. Excluding the psychologic symptoms, it is evident that the physical ones, such as facial pallor, dyspnea and, especially, vomiting, are results of action of the sympathetic nervous system. According to previous studies, vomiting is produced by strong contraction of the abdominal wall, opening of the cardia and closing of the pyloric sphincter. The contraction of the abdominal wall in the rabbits was produced by stimulation of the sympathetic nerves. These observations indicate that seasickness in general is produced by strain on the sympathetic nervous system. Great care was taken with the use of sodium bicarbonate in man to obviate any deleterious effects.

A man aged 20 volunteered for this study. He was born of a fisherman's family, but because of constant seasickness was not able to perform the only job available to him. Even riding in trains or steamers made him nauseated. Physical examination indicated that his condition was essentially normal. When he was placed in a rotating chair, or if he rode in an elevator, he experienced profound nausea, vomiting and dizziness. He was given an intravenous injection of 40 cc. of 5 per cent solution of sodium bicarbonate, and the tests with the rotating chair and elevator were repeated. This time he had no reaction and was not even disturbed by a boat ride on very rough water.

From a battalion of 474 men in the Japanese Army, 40 were selected who complained of chronic seasickness, as well as 6 who professed to being seaworthy. All these men received the Aschner test, in which both eyes were pressed to the extent that pain was felt, and then the pulse rates were measured. Those with a decrease in pulse rate from 0 to 4 were classed as having tension of the sympathetic type; those with a decrease from 5 to 9, as normal, and those with a decrease from 10 to 15, as having tension of the parasympathetic type. Of the 40 men who were chronically seasick, 24 were found to be in the first class and 16 in the third. The 6 men who were seaworthy were all in the second class. Of the remaining 428 of the battalion, 327 were normal, in the second class, and 101 were in the third class. Judging from this test, it may be said that all persons with tension of the sympathetic type are subject to seasickness, but that only some with tension of the parasympathetic type are apt to get seasickness. Twelve of the 24 with the tension of the sympathetic type and 8 of the 16 with tension of the parasympathetic type were given 40 cc. of 5 per cent solution of sodium bicarbonate intravenously. Then these 40 men and the 6 seaworthy, together with the rest of the battalion, were exposed to the hardships of a long boat trip in a very heavy storm. Most of the men aboard became extremely seasick, even those who considered themselves seaworthy. But all the 20 men who received the injections remained well, took meals as usual and helped take care of the sick.

Another interesting observation was made when a young man aged 22, who was dying of nasal sarcoma, was given 40 cc. of 5 per cent solution of sodium bicarbonate intravenously. He died two weeks later, and histologic section showed that the otolithic crystals had been dissolved.

CONCLUSION

Sodium bicarbonate injected intravenously can prevent motion sickness from occurring in man, probably by dissolving the otolithic crystals. It is also suggested that this injection may possibly be of value in Ménière's disease.

PENICILLIN IN CHRONIC OTITIS MEDIA

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DURING the time that penicillin was first being used in the treatment of practically any and all types of infections, it was felt that it would be desirable to determine exactly what might be expected from the sole use of this new antibiotic agent in the treatment of chronic otitis media. After the initial experimental stages had given a fairly accurate estimate of the value of the drug against the various acute infectious diseases, it was pretty generally agreed among otologists that penicillin was a substance of real merit in the treatment of acute otitis media and its many complications. This is now an established fact.

The management of the chronically discharging ear has varied greatly over the years. Experience with a succession of nonsurgical methods has been inconsistent and left much to be desired in the way of end results. Although it was realized that the conditions which obtain in chronic disease of the middle ear differ in several ways from those in acute infection, it was considered that a controlled study would be advisable. Hence a study of the systemic use of penicillin was started. To obtain a group of patients with chronically discharging ears hospitalized under control for a sufficient length of time and with adequate dosage of penicillin to provide an estimate of the usefulness of the drug, this study was made in a military hospital.

A total of 82 patients were treated according to a rather rigid and set type of regimen. Unfortunately, when the final charts were being assembled for the statistical survey it was found that many were missing, the patients having been transferred for various reasons or discharged from the service and their charts forwarded to the proper agency. It is felt, however, that the 40 cases for which data were available provide a representative picture of the group as a whole.

The patients were selected from otolaryngologic patients seen routinely in the clinic of a large general hospital. Patients with obvious surgical conditions, such as cholesteatoma or definite destruction of bone, or with complications were not considered for penicillin therapy. A minimum time requirement of two months was set before the condition was considered to be chronic. This period might be considered

Presented as a candidate's thesis to the American Laryngological, Rhinological and Otological Society, Inc., 1949.

short, but it was felt that such a condition could no longer be classed as acute. The longest period of discharge in these cases was twenty-nine years. The hearing in each case was recorded by both an audiometric study and use of the whispered and the spoken voice. At the time of this survey, use of the whispered voice was the method of choice. Unfortunately, since the patients were a more or less transient group, it was next to impossible to get an accurate follow-up of the hearing over a prolonged period. The type of perforation was recorded. Some marginal perforations were included, even though it was realized that these are sometimes considered to be an indication for surgical treatment. The results obtained in cases of marginal perforation would seem to confirm this opinion. The duration and type of discharge were noted in each case and also whether the discharge had been continuous or intermittent. It was felt, however, that a number of cases in which there was a history of an intermittently discharging ear should be placed in the continuous class, since the ears had never been completely dry. The patient usually described the ear as dry during that period in which the discharge was not actually draining from the auditory canal or was not spotting the pillow at night. The organisms cultured were found to correspond to those isolated in similar groups of patients with chronic otitis which have been reported many times in the literature. Studies of sensitivity of the organisms and determinations of penicillin levels were done in many of the cases. Unfortunately, since the hospital was running at peak capacity, laboratory facilities did not permit the carrying out of these studies in all cases. Undoubtedly, sensitivity studies in each case would have been of value in estimating the expected result. The therapy which had been used previously in these cases varied widely, including all the methods and drugs which had been in vogue in recent years.

Roentgen studies were made but were found to be of limited value in the interpretation of the results to be expected from treatment. Serial roentgenograms were made in the first cases to be studied, and, for the most part, they showed no change either during or following chemotherapy.

The dosage of penicillin remained constant throughout the treatment period in each case. Twenty-five thousand units of the sodium salt was injected every three hours, day and night. It was fortunate that in no case did a reaction occur of a serious enough nature to cause discontinuance of the drug. This was an interesting sidelight in view of the known impurities in the manufactured product at that time. To my knowledge, this was one of the first attempts to give the drug in what was then considered a massive dose over so prolonged a period. Ten thousand to 15,000 units every three or even every four hours was considered to be the optimum dose at that time. It was because of

the known rapid fall of the penicillin concentration in the urine during the third hour that this larger dose was considered preferable. It was also determined at this time that the resistance of certain organisms to the drug might increase as therapy progressed, and this was the first indication that the dosage schedule, even in the treatment of acute otitis, should not be decreased or "tapered off" as clinical improvement was shown. Decreasing the dose was the method accepted by most physicians in 1942 and 1943. In the light of present day knowledge it is felt that if the dosage were doubled or even tripled clinical results might be further improved.

All patients were allowed ward privileges and a regular diet. No other local or systemic medication was given. The ears were cleansed and inspected twice each week, and any progress noted. Patients were visited on ward rounds each day.

Results were classified as "no results" if there was no obvious change either during or following the treatment; "fair" if there was slight but definite lessening of the amount of discharge and the improvement was maintained; "good" if there was definite clinical improvement as determined by almost complete cessation of the discharge and, in some cases, by improved hearing. The patients became aware of this improvement during the follow-up period of two months. If there was a return to the former clinical status, the results were then classified as either "no results" or "fair." "Excellent" was reserved for those cases in which the ear became perfectly dry and remained so; hearing at times improved, and in some of the cases there was closure of the perforate tympanic membrane. The minimum observation period was two months, and the maximum was two years.

For the forty-one ears treated, the results compiled were as follows: no results, 11; fair, 6; good, 8, and excellent, 16. Interpreted in terms of percentage, the "no results" and "fair" groups made up 41 per cent of the total and the "good" and "excellent" groups 59 per cent. The "excellent" group alone accounted for 39 per cent of the total. Further interpretation of the various groups revealed that in the "no results" group there were three marginal perforations, five central, one anteroinferior, one anterosuperior and one posteroinferior. The last three could readily be classed with the five central perforations. It is interesting to note that among the entire group of forty-one ears all but one of the marginal perforations fell into the "no results" group. This one exception on culture revealed a pure strain of coagulase-positive hemolytic Staphylococcus aureus and also was just inside the minimum time interval of two months. It was concluded from this fact that the drug was probably of no benefit in case of marginal perforations of long standing. Nothing definite in regard to the cultures in this group could be distinguished except that in a majority of the cases as one would

expect, Proteus vulgaris was isolated. It was noteworthy that in this group there were several cases in which the primary organism had been a hemolytic streptococcus which had not responded to previous therapy, whereas in the other groups a response was obtained. Nothing remarkable was noted in regard to previous therapy in this group except that in no instance could it be considered that adequate antibiotic or chemotherapy had been given; this was true also of the other groups. The roentgenologic findings were noncontributory.

Results for six ears were listed as "fair." Of the six, four were listed as having central perforations, and two had perforations of the pars flaccida. The duration of aural discharge had been from five months to three years. In this group a significant feature was that five out of the six were of the continuous drainage classification. As in the first group, interpretations of the roentgenograms were of little aid. Four of the six had had previous therapy with one or more of the sulfonamide drugs, without improvement.

Results for eight ears were classified as "good." Six of the eight were found to have central perforations; one perforation was marginal, and one was not recorded. The duration of aural discharge varied from two months to five years. In six of the eight the duration of otorrhea had been of less than eighteen months' duration and in the remaining two of four and five years' duration. Seven of the discharges were classed as being of the continuous purulent type. Cultures revealed a gamma streptococcus as the predominant organism in three ears and Staph. aureus in two. Peculiarly, one of the ears from which a gamma streptococcus was isolated had had previous antibiotic treatment with penicillin intramuscularly every three hours for fourteen days with no results. It was impossible to learn the number of units given in each dose. This may have had something to do with the poor result, or, as recently discovered, the streptococcus may have become sensitive with the growth of allied organisms.

In sixteen of the ears results were classed as "excellent." The duration of the otorrhea varied from three months to twenty-six years. Of the sixteen ears, only four were classed as having discharged for one year or less. It is notable that in this group all perforations were of the so-called "central" type, with no involvement of the margin or the pars flaccida. Of the discharges, ten were of the intermittent variety, four continuous and two not classified. The fact that almost two thirds of the discharges in this group were of the intermittent variety brought up the question whether the excellent results might represent just another period of remission or quiescence. However, several of the patients were followed for periods up to two years and there was no evidence of recurrence. It would have been of interest to follow this group especially for a much longer period to see what the rate of

Summary of Data on Forty Cases of Chronic Suppurative Otitis Media

Case No.	Hearing	Ear Involved	Type of Perforation	Discharge		Organisms Cultured	Previous Therapy	Roentgen Findings	Total Dose of Penicillin, Million Units	Results*
				Duration	Type					
1	L 7/15	Left	Posterior inferior margin	29 yr.	Profuse intermittent	P. vulgaris; Staph. albus; gamma streptococcus	Alcohol; sulfonamides; irrigations	Sclerosis; no visible cells	4	N
2	R 6/15	Right	Large central	28 mo.	Moderate mucopurulent, continuous	Hemolytic Staph. aureus, coagulase, positive; Ps. aeruginosa, diphtheroids	Sulfonamides for 2 weeks	Poorly defined cells; no destruction; moderate sclerosis	4.5	F
3	L 5/15	Left	Posterior superior margin	18 mo.	Slight purulent	Shigella sonnei	Sulfonamides for 2 weeks; irrigations	No cell outlines; dense sclerosis	4	N
4	R 7/15 L 12/15	Both	Large central	4 mo.	Profuse purulent, continuous	P. vulgaris (R); Neisseria catarrhalis; diphtheroids (L)	Sulfonamides; daily care	No destruction; poor development; left, few cells; right, none	3.8	Left N Right E
5	R 6/15	Right	Anterior inferior	4 mo.	Moderate purulent, continuous	Beta streptococcus; Ps. aeruginosa	Alcohol; sulfonamides by mouth; penicillin for 5 days	Poor development; cloudy; pneumatic; no destruction	4	N
6	R 1/15	Right	Small central	16 mo.	Moderate purulent, continuous	Hemolytic Staph. aureus, coagulase positive; gamma streptococcus	Not known	Very cloudy; no decalcification; no destruction	4	E
7	R 15/15	Right	Small posterior margin	2 mo.	Slight suppuration, continuous	Hemolytic Staph. aureus, coagulase positive	None	Poor development; poor cell structure; slight sclerosis	4	G
8	L 6/15	Left	Anterior superior	3 mo.	Slight suppuration, continuous	Beta streptococcus; P. vulgaris	None	Little cellular structure of diploe; severe sclerosis	4.575	N
9	R 7/15	Right	Moderate posterior inferior	15 yr.	Moderate purulent, intermittent	Gamma streptococcus; Staph. albus	Ear drops; sulfonamides orally and locally	Poor development; sclerotic; slightly enlarged antrum	4	E
10	L 3/15	Left	Moderate central	2 yr.	Moderate purulent, intermittent	Alpha streptococcus; Ps. aeruginosa	Local	Chronic progressive sclerosis	4	E
11	R 13/15	Right	Small posterior	1 yr.	Moderate purulent, intermittent	Alpha streptococcus; Ps. aeruginosa	Penicillin orally; locally 3 days	Small; poorly developed; cloudy; antrum enlarged	4	E
12	Both 15/15	Right	Anterior inferior	5 mo.	Continuous purulent	P. vulgaris	Sulfadiazine orally, amount not known	Cloudy mastoid; no evidence of destruction	3	E
13	Both 15/15	Right	Large central	16 yr.	Purulent, intermittent continuous for 4 mo.	Staph. albus; P. vulgaris	Boric acid and alcohol drops	Not available	3.6	E
14	L 6/15	Left	Small; shrapnel	3 yr.	Purulent, continuous	Aspergillus glaucus; P. vulgaris	Sulfadiazine orally 12 days	Absence of cell development	4.15	F
15	Both 15/15	Both	Large central	4 mo.	Purulent, continuous	Not known	Sulfonamides orally	Evidence of bilateral breakdown of cells	3.6	N
16	R 15/15	Right	Moderate anterior inferior	17 yr.	Purulent, intermittent	Hemolytic Staph. aureus, coagulase positive	Boric acid and alcohol drops	Sclerosis; few cells; slightly enlarged antrum	4	E
17	L 6/15	Left	Small; shrapnel	Unknown	Seropurulent, continuous	A. glaucus	Not known	Sinuses poorly developed; sclerotic	4.2	G
18	R 15/15	Right	Small posterior central	10 yr.	Foul purulent, intermittent	Alpha streptococcus; P. vulgaris	Boric acid and alcohol drops	Diploic periantral sclerosis	3.8	E
19	L 14/15	Left	Large central	18 mo.	Foul purulent, continuous	P. vulgaris; diphtheroids	Penicillin intramuscularly 7 days; boric acid drops	Poor development; sclerotic irregular antrum	4	G
20	L 2/15	Left	Large central, traumatic	7 mo.	Profuse purulent, continuous	Staph. albus; gamma streptococcus; Aerobacter aerogenes	None	Cloudy; well developed calcified septums near sinus knee	3.8	G
21	L 1/15	Left	Large posterior margin	2 yr.	Moderate purulent, intermittent	Beta streptococcus; P. vulgaris	None	Poor development; slight cloudiness; no destruction	4.475	N

22	R 13/15	Right	Posterior inferior	4 yr.	Moderate purulent, intermittent	Alpha streptococcus; A. aerogenes	None	Not available	4.760	E
23	R 15/15	Both	Moderate posterior central	5 mo.	Mucopurulent, continuous	Staph. albus; P. vulgaris	Penicillin intramuscularly 3 days; sulfadiazine 7 days	Slightly thick cell walls; moderate sclerosis	4	N
24	L 5/15	Left	Large oval central	26 yr.	Thick purulent, intermittent	Not known	Boric acid and alcohol drops	Sclerotic with very few cells	4	E
25	L 13/15	Left	Large inferior central	5 mo.	Thick purulent, continuous	A. aerogenes; diphtheroids	Sulfonamides orally; alcohol drops	Diploic marked periantral sclerosis	4	F
26	Both 15/15	Right	Moderate central inferior	18 mo.	Purulent, continuous	Hemolytic Staph. aureus, coagulase positive	Sulfonamides orally 1 month and later 2 weeks	Sclerosis with few visible air cells	4	F
27	R 12/15	Right	Moderate; shrapnel	10 mo.	Purulent, recurrent	Not known	Attic lavage; alcohol drops	Moderate sclerosis; moderately thick cell walls	4	E
28	R 2/15	Right	Moderate central	15 yr.	Purulent, intermittent, 5 mo. continuous	Anaerobic beta streptococcus	Sulfonamides orally; alcohol drops	Sinuses poorly developed; slightly cloudy; slight sclerosis	3.8	HE
29	L 0/15	Left	Large central	7 mo.	Mucopurulent, continuous	Hemolytic Staph. aureus, coagulase negative	Sulfonamides orally; penicillin locally	Sclerotic, slightly irregular antrum	3	N
30	R 10/15	Right	Moderate anterior central	3 mo.	Thin purulent	Beta streptococcus; Ps. aeruginosa	Sulfonamide powder; alcohol drops	Slight clouding of cells; no destruction	3.5	HE
31	L 3/15	Left	Moderate central	2 mo.	Profuse purulent	Ps. aeruginosa overgrown	None	Moderate clouding; no destruction	4	N
32	Both 15/15	Left	Moderate posterior central	16 yr. intermittent; 5 yr. continuous	Purulent	Hemolytic streptococcus; hemolytic Staph. aureus	Penicillin intramuscularly 3 days	Poor development; slight clouding; antrum enlarged	4	E
33	Both 10/15	Left	Moderate posterior central; due to bomb blast	6 mo.	Purulent, continuous	Gamma streptococcus; Ps. aeruginosa	Syringing	Cells slightly cloudy; no destruction	4	F
34	R 8/15 L 6/15	Both	Large central (bilateral)	L 15 yr. R 6 mo.	Purulent, intermittent (left); continuous (right)	P. vulgaris; Ps. aeruginosa (bilateral)	Penicillin intramuscularly 4 days; local drops	Moderate sclerosis; no destruction; enlarged antrums	4	N
35	Both 15/15	Right	Posterior central, traumatic	5 mo.	Purulent, hemorrhagic, continuous	Beta streptococcus; Ps. aeruginosa	Sulfonamides locally; alcohol drops	Sinuses well developed; slight clouding; slight decalcification	3	HE
36	L 10/15	Left	Moderate central	1 yr.	Purulent, intermittent	Hemolytic Staph. aureus	"Listerine" (antiseptic solution N.F.) drops; ultraviolet rays	Very sclerotic; antrum enlarged	4	E
37	Both 15/15	Left	Small posterior inferior	3 yr.	Purulent, continuous	Staph. albus; A. fecalis	Sulfonamides locally; cleaning	Well developed; cloudy; no destruction	3.6	E
38	R 8/15	Left	Large central	6 mo.	Purulent, continuous	Gamma streptococcus; Ps. aeruginosa	Penicillin every 3 hours for 14 days; sulfonamide powder	Poor development; slight clouding; no destruction	3.6	F
39	R 14/15	Right	Small anterior inferior	5 yr. intermittent; 1 yr. continuous	Purulent	Hemolytic Staph. aureus, coagulase positive	Powder, hydrogen peroxide; alcohol drops	Moderate sclerosis; no destruction	4	F
40	R 12/15	Right	Moderate central	4 yr.	Purulent, continuous	Gamma streptococcus	Sulfonamides orally 7 days	Moderate sclerosis; slightly enlarged antrum	4	F

* N indicates no results; F, fair results; G, good results; E, excellent results; HE, healed membrane excellent results.

recurrent otorrhea would be. The bacteriologic findings were interesting in that from fourteen of the sixteen ears a streptococcus or a staphylococcus, or both, presumably sensitive to penicillin, were cultured. One ear was reported to have yielded a pure culture of Proteus vulgaris and yet responded to therapy. In this group there is also noted a large number of ears with secondary invaders, five with Pseudomonas aeruginosa, four with P. vulgaris and one with fecalis. None of these organisms are sensitive to penicillin. It is difficult to explain the cessation of discharge in view of this known fact. Perhaps it was because of the thorough cleaning given each ear at the time of inspection. Had local therapy been used in conjunction with the antibiotic agent it is felt that the percentage of good or excellent results might have been higher.

It has been noted that when there is traumatic perforation of the tympanic membrane accompanied with infection, the tendency of the membrane to heal is greater. Three tympanic membranes in this group were healed, and in each of these the culture revealed the beta streptococcus as the primary organism. In this group alone it was felt that the roentgenograms might have been of some aid, as each of the three showed either no sclerosis or clouding or only slight sclerosis and mild clouding.

SUMMARY

Penicillin given intramuscularly over a prolonged period was found to be of definite value in the treatment of certain cases of chronic otitis media. Ears with chronic discharge ranging from two months to twenty-nine years' duration have remained dry for as long as two years following treatment. In a small percentage of cases there was not only cessation of the otorrhea but healing of the tympanic membrane. Penicillin was not given to supplant surgery in the treatment of chronic otitis; however, in this selected group of patients it was found to give a greater than 50 per cent chance of obtaining a dry ear and maintaining it for two years or longer.

My later experience with the use of penicillin locally in cases of chronic otitis media would indicate that a higher per cent of good results may be obtained from the combined use of this antibiotic drug.

Further study of the use of antibiotics in chronic diseases of the ear is indicated to determine the degree of return of hearing and also the rate of recurrence when followed over a period of years.

CONCLUSIONS

1. The intramuscular use of penicillin alone offers a better than 50 per cent prospect of obtaining a dry ear in the treatment of selected cases of chronic otitis media.

2. It is of doubtful or no value in the group of so-called marginal perforations.

3. One cannot expect as good results when it is used in those cases in which the discharge from the external canal is interpreted as continuous.

4. Best results from the use of penicillin will be obtained in the central type of tympanic perforation and also in cases in which there has been otorrhea for less than eighteen months.

5. When used in cases in which the predominant organism is the beta streptococcus the membranum tympani will have a greater tendency to heal.

6. Roentgen examination is not helpful in the selection of cases with possibly one exception; when little sclerosis is shown, the chances of a good end result are greater.

615 Anderson Bank Building.

MANAGEMENT OF ACUTE LARYNGOTRACHEOBRONCHITIS

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IN 1908, Chevalier Jackson directed the attention of the physicians of America to a disease entity which has come to be known as acute laryngotracheobronchitis. As a pioneer in endoscopy, Jackson was afforded the opportunity of viewing through the bronchoscope the nonmembranous character of this disease as it affected the larynx, trachea and bronchi in a number of children who appeared clinically to have diphtheria. He described the pathology as differing from that of diphtheria in that the mucosa was more edematous and the secretion thick and tenacious, tending to form crusts and plugs and often leading to atelectasis and death.

The disease in its severest form was observed most frequently in children under 3 years of age, whose air passages are actually, as well as relatively, smaller than those of older children. When a normally small airway was attacked by an inflammation characterized by swelling of the loose subglottic tissue and the formation and accumulation of thick, gummy, gluelike secretion, with absence of the cough reflex, one could easily understand the degree of obstruction to the passage of air to the lungs in many of these patients.

Without the help of drugs of specific action, treatment was limited to supportive measures and to efforts directed toward maintaining a free airway. These, in the main, consisted of (*a*) forcing of fluids and addition of moisture to the inspired air; (*b*) bronchoscopy, with suction and removal of plugs with forceps; (*c*) tracheotomy; (*d*) suction with a soft rubber catheter passed through a tracheal cannula, and (*e*) dropping of solution into the trachea, followed by suction.

It was hoped that if the airway could be maintained for a time the defensive forces of the body would become active and overcome the infection. Very often these measures were not adequate, and it was not surprising that published reports of such cases revealed a mortality rate of 50 per cent or higher. Actually, the mortality rate of all such cases throughout the country must have been much higher, for hundreds of cases were never reported.

Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948.

In recent years, or since the introduction of antibiotic drugs, the few published reports show a considerable drop in the mortality rate. In spite of these favorable reports, the disease in its severe fulminating form has not been brought under control in all cases. Certainly, the experience that we at Children's Hospital have had with cases of laryngotracheobronchitis has not been entirely satisfactory, as the following report will show.

This report does not include all these cases, only those occurring during an eight year period, from 1940 to 1947, inclusive, in which a tracheotomy was required. It may be assumed that nearly all of the patients who did not require operation lived. The histories of 10 of 12 patients in whom the condition was fatal were reviewed for the purpose of determining the cause of death. Postoperative accident was the

Cases of Tracheotomy

Year	Number	Deaths
1940	12	2
1941	6	1
1942	8	2
1943	7	0
1944	18	4
1945	8	0
1946	2	0
1947	3	3
Totals	64	12
Mortality rate	18 + %	

cause of death in 1; bronchial obstruction, atelectasis and pneumonia in 2; bronchial obstruction in 3; pneumonia in 2, and emphysema and pneumothorax in 2. Seven of the 10 patients died within one day after admission to the hospital; 72 per cent of the patients were under 2 years. This review of a small number of cases points to bronchial obstruction as the most frequent cause of death.

Tracheotomy alone, or combined with bronchoscopy, with removal of plugs with forceps and suction, will not always clear the airway sufficiently to permit an adequate supply of oxygen to reach the lungs. In our experience, obstruction has been the chief obstacle to successful treatment. It has been suggested to us that the lungs be by-passed for a time by the introduction of oxygen into the vessels. So far we have not had the courage to attempt this. Perhaps we are omitting some important step in our treatment. In order that the members may know what measures have been employed, the remainder of the paper will be devoted to their discussion.

MATERIAL AND METHODS

On admission to the hospital, the child is placed in a tented crib supplied with moisture and oxygen and given an injection of penicillin. If he is badly in need of oxygen, he is placed in an oxygen tent while preparations are being made for tracheotomy. In the event that the child rallies quickly, operation is deferred and he is transferred to the tented crib and watched. If the improved condition continues, he is kept in the crib.

Humidified air has long been considered helpful in the treatment of this condition, but the manner of its administration has not always been satisfactory. The old-fashioned croup kettle is not suitable for these cases; too much time is lost in getting up the steam; besides, the room or the enclosure becomes unbearably warm. Humidifiers placed in a room have not been entirely satisfactory. Their action also is too slow; their motors get out of order; pools of water collect on the floor, and electrical connections make the work of the nurses hazardous.

The setup that we have been using for three or four years, and find very satisfactory, consists of a draped crib into which water and oxygen are sprayed; it has the following advantages:

1. The equipment is quickly set up, and in a few minutes an adequate amount of moisture mixed with oxygen is delivered to the patient.

2. It does not get out of order.

3. There are no electrical connections.

4. The air in the tent is kept cool, 70 to 75 F.

5. The amount of oxygen is sufficient for the need in most cases, 25 to 40 per cent by volume.

6. Additional oxygen or oxygen and helium can be supplied directly to the tracheal cannula, if needed.

We believe that since the use of this setup the tendency toward formation of bronchial plugs has been lessened and that it has been an important factor in reducing the number of cases in which a tracheotomy would be required.

This setup has been well received by the pediatricians of our hospital, as many as seven sets having been seen in operation at one time. While we believe that we have found a satisfactory method of supplying moisture, so essential in counteracting the formation of crusts and plugs, it must always be kept in mind that it is the amount of oxygen that reaches the alveoli of the lungs that is important, rather than the amount flowing into the tent.

In most cases, the amount of oxygen being delivered to the patient will be adequate. The plastic canopy draped over the top of the crib is allowed to hang free at the bottom to permit a free exchange with the air in the room. If this precaution is observed, the accumulation of carbon dioxide in the tent will be negligible.

Dr. John Rathbun, the chief resident at Children's Hospital, is having a small compartment fitted into the tent which, it is believed, will make it possible to add the use of penicillin mist to the present method of administering humidified oxygen. Penicillin in this form has been used in a few cases with good effect.

It takes an experienced observer, one who has spent many hours at the bedside of these patients, to appraise their condition. Even then, his judgment may be faulty. Determinations of the oxygen content of arterial blood may be helpful. Unless the respiratory rate is decreasing, the color of the child is improving, there is less tugging and the child is able to rest comfortably, he may be slipping into a dangerous state of anoxia, so well described by Galloway.

Drugs.—Without the aid of present day drugs, the mortality rate would still be high, and so it is important that they be used promptly and in adequate dosage.

Penicillin is our first choice, alone or with sulfadiazine. Streptomycin has been added in a few cases in which an influenzal infection was suspected. Jackson has cautioned against the use of atropine and codeine. Phenobarbital has occasionally been used.

Hydriodic acid syrup given late in the disease seems to help in thinning the secretion.

Tracheotomy.—Except at the hands of a few experts, tracheotomy on a small child is a hazardous procedure. Any one considering a tracheotomy should read Neffson's article.[1] It would be well to give heed to his list of indications for tracheotomy, and to his caution against too much dissection. Neffson's assertion that audible stridor is not always an indication for tracheotomy tallies with our experience. With regard to stridor, Neffson stated: "It was when the stridor became 'muffled,' aphonic, that we began to worry, because it meant that the airway was becoming narrowed by edema or secretion or membrane or a combination of them."[1] He lists his indications for tracheotomy as follows:

"Signs of extreme obstruction
Restlessness
Cyanosis—pallor
Deep retractions
Absence of breath sounds
Anxious facies

Signs of exhaustion
Tachycardia; impalpable pulse; heart failure
Tachypnea—rapid, shallow breathing
Hyperpyrexia—from 105 to 107 F.
Stupor; coma; convulsions"

Technic in the performance of tracheotomy is very important. Usually, the child's condition is desperate, and there is a tendency, therefore, to hurry the operation. The tracheotomy will be greatly facilitated by the passage, first, of a small bronchoscope or, if one lacks experience in bronchoscopy, of a Mosher life-saving tube. Through the bronchoscope, secretion may be suctioned, thus clearing the airway for the admission of oxygen if needed during the operation. This preliminary step will enable the operator to work more leisurely; with the patient under local anesthesia, very little dissection will be necessary because the trachea is held fixed in the midline and nearer the surface. Dissection of the cricoid cartilage must be avoided, and Neffson warned against stripping the pretracheal fascia so that air might be permitted to enter the chest.

Postoperative Care.—After-care when tracheotomy is performed is as important as the tracheotomy itself. After a satisfactory airway has been established, the next problem is to prevent its later obstruction by secretion drying and accumulating in the trachea and bronchi. To combat such a tendency, it is very important to have a nurse specially trained in this work constantly at the patient's bedside. No one appreciates better than she the importance of changing the inner cannula when it becomes plugged; aspirating secretions to maintain a free flow of air; forcing liquids, and maintaining a high degree of humidity and oxygen in the crib at all times.

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1. Neffson, A. H.: Tracheotomy in Cases of Acute Obstructive Nondiphtheritic Infections of Larynx, Trachea and Bronchi: General Study, with an Analysis of One Hundred and Twenty-Six Consecutive Cases Occurring During the Past Decade, Arch. Otolaryng. **36**:773 (Dec.) 1942.

Members of the profession whose work is confined largely to laryngology and endoscopy have an advantage in this respect. Other physicians often have to rely on the good judgment of a head nurse to direct properly and to supervise closely an inexperienced student nurse, rather than to engage a graduate nurse without experience who will not accept advice. Such an arrangement will require close vigil on the part of the physician, a not uncommon experience for him during these latter years.

Attention to details is important, and, if observed, all but a few patients will be brought safely through a disease in which the death rate was formerly high.

CONCLUSION

The measures outlined in this paper, when used early and adequately, have proved effective in greatly reducing the mortality rate in cases of acute laryngotracheobronchitis. These measures represent a pooling of the experiences of many of our colleagues.

It is hoped that the discussion which follows will tell us how to handle the not so rare fulminating type, which remains an unsolved problem.

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ABSTRACT OF DISCUSSION

Dr. L. H. Clerf, Philadelphia: At the clinic with which I am associated, there are not as many cases of acute laryngotracheobronchitis now as there were ten or fifteen years ago, the infection does not appear so severe, tracheotomy is required less frequently and the mortality rate is low. Also, the condition now is more often seen earlier, and this is an important factor in treatment and in end results.

The plan of therapy at my clinic differs little from that presented by Dr. Simpson. With the consideration of diphtheria and a foreign body as diagnostic possibilities, penicillin therapy is started, and the patient is placed in a cool, humidified atmosphere to which oxygen is added. An adequate fluid intake is maintained. If dyspnea is severe on the patient's admission, or if dyspnea progresses in spite of therapy, tracheotomy is performed without delay. It is a mistake to defer tracheotomy and consider it as a last resort. When tracheotomy has been performed, one must not wait for laryngeal obstruction. The nurse should change the inner cannula at stated intervals, even when no apparent obstruction exists. In addition, isotonic sodium chloride solution, with or without penicillin, should be instilled at stated intervals to prevent crusting of secretions. Suction with catheter should be employed only if the child is unable to cough up the solution and secretions. Trauma to the tracheal mucosa, with bleeding induced by the catheter suction, increases the tendency toward crusting.

In connection with tracheotomy, I wish to emphasize the importance of leaving the wound open. Too many violate the important surgical principle never to close infected wounds and to sew the skin snugly around the cannula.

Humidification is extremely important. Dr. Simpson's method is an ingenious and an excellent one. I do not consider it necessary to maintain a humidity of 90 to 100 per cent. One can get a humidity of about 70 per cent in an oxygen tent in the presence of a cool atmosphere, and that seems adequate. I have discussed with representatives of manufacturers of oxygen tents the desirability of installing

an auxiliary aid for humidification, which would simplify the problem immeasurably. Too often nurses are not competent to operate an assortment of gadgets, and, from an economic standpoint, patients often cannot have physicians, nurses and maintenance men in attendance.

I wish to compliment Dr. Simpson on the excellence of his presentation.

DR. PAUL H. HOLINGER, Chicago: Acute laryngotracheobronchitis continues to be one of the urgent medical emergencies. Proper management depends on the cooperative efforts of the pediatrician, the laryngologist and the resident staff. As Dr. Simpson has mentioned, the nursing care of infants in whom laryngotracheobronchitis is developing is almost a specialty in itself.

Dr. Simpson has pointed out that the introduction of antibiotic drugs has been followed by a decided drop in the mortality rate. These agents are now so continuously used by the pediatrician at the onset of the infection that the incidence may appear to be diminishing. However, as he mentioned, the not so rare fulminating type of case remains a difficult problem. This disease constitutes a medical emergency and is treated as such. At the Children's Memorial Hospital, admission routine is by-passed, the infant is placed immediately in the "steam room" and chemotherapy is started at once. Both penicillin and sulfathiazole are administered and administrations continued until the throat cultures indicate that one or the other of these agents is no longer necessary. Streptomycin is used in addition in the more fulminating cases in which the influenzal organism is often found to be the causative agent. My associates and I have found the sulfonamide drugs much more effective than penicillin and have often noted a favorable response following their administration when penicillin alone had been used without appreciable benefit. This use, obviously, is dependent on the causative organism.

Dr. Simpson has devised a unique method of supplying humidity. Humidity is second in importance to chemotherapy in the management of acute laryngotracheobronchitis. We still prefer the mechanically humidified rooms for this purpose, with the room temperature between 70 and 75 F. and the relative humidity above 90 per cent. The rooms set aside specifically for this purpose are rarely idle. One wonders whether the relative humidity in the tents can be kept this high when they have to be opened frequently for necessary nursing care. With adequate humidity, deaths due to bronchial obstruction, the most frequent cause in the cases reported, should be almost completely eliminated.

We agree with Dr. Simpson that if surgical relief for respiratory obstruction becomes necessary, bronchoscopic aspiration and tracheotomy with the bronchoscope in place are the methods of choice. Intubation in too many instances is not satisfactory. The reports in the recent literature that tracheotomy with a bronchoscope in place is followed by mediastinal emphysema and pneumothorax are provocative of further investigation and discussion. We feel that these complications, when they arise with the use of this technic, are due to too low a tracheotomy, since the hyperextended position of the head draws the thoracic portion of the trachea well up into the neck. Then, as the bronchoscope is withdrawn and the head returns to its normal position, the tracheal incision lies within the thorax. Subsequent coughing forces the air into the mediastinum or the pleural cavity.

The tent Dr. Simpson has devised seems most ingenious and, possibly, with the addition of penicillin mist, may have certain advantages. I should like to ask him whether he has carried on humidity readings in the tent and whether he feels that the tent can be kept sufficiently closed during nursing and aspirations through the tracheotomy tube to keep the humidity from dropping. We believe that a special room mechanically humidified permits a more constant, higher humidification and thus is more likely to prevent the formation of bronchial plugs.

DR. GABRIEL TUCKER, Philadelphia: Certainly, my associates and I agree with Dr. Simpson and the discussers that the tracheotomy should not be delayed. For the past three or four years we have used a special technic for the insertion of the bronchoscope, that of putting a pack, in which we use antibiotics, penicillin or powdered sulfanilamide, around the tube. We have had no cases of infection of the neck, and no cases of emphysema. The prevention of these complications is most important. We have a method by which these complications are practically one hundred per cent avoidable. I believe the method is not in general use, but my associates at the University of Pennsylvania, Dr. Atkins and Dr. Lee, have used it in hospitals with which they are associated. It enables one to make a very short incision in the neck; one does not expose the whole front of the neck or get down into the mediastinum. The incision is made just large enough to expose the trachea; then a short incision is made in the trachea itself. Then, if a pack is placed in this incision and the tube tied tightly around the neck, emphysema or infection will be prevented by the antibiotics impregnated in the pack. The tube is wrapped with narrow gauze impregnated with either sulfanilamide or penicillin, and a practically clean wound results.

DR. THOMAS GALLOWAY, Chicago: I should like to emphasize the place of postural drainage in treatment. Dr. Simpson has the patient lie flat during drainage. I think this is a grave mistake. Since my associates and I have used postural drainage with irrigation, we practically never do a bronchoscopy. At least a 20 degree angle is necessary to achieve postural drainage. This is the normal declivity of the trachea and bronchi from the body axis. In order to get postural drainage, the body must be elevated at least 25 degrees, and this is seldom done. With this elevation, and with the use of 3 per cent solution of sodium bicarbonate through the tracheotomy tube to loosen mucus and plugs, followed by isotonic sodium chloride solution, bronchoscopy to remove crusts and plugs will seldom have to be done.

The Walton mechanical humidifier, in which a tube is led up into a croup tent, provides excellent humidification; we have seen repeatedly, in cases in which this humidifier had not been used previously but had been instituted, that the crusting completely disappeared.

The antibiotics are indicated, but the mechanical factors are very important. Some of these infections undoubtedly are caused by a virus.

We have now had 15 consecutive cases at the Evanston Hospital without a death. Part of this result is due to better cooperation on the part of other physicians, who realize that any child with beginning obstruction should be hospitalized and should be seen early by a laryngologist. We believe that we no longer see many cases of the fulminating type. The other factor is recognition of the fact that anoxia and the effects secondary to obstruction with negative intrathoracic pressure very quickly make the condition irreversible, so that when tracheotomy is to be done there must be no delay.

DR. DAVID DAVIS, Washington, D. C.: Something besides the use of steam and antibiotics, which may or may not be effective, should be done for such children while it is being determined whether a tracheotomy is needed. We physicians sometimes fail to do a certain thing which was advocated by Baum several years ago. He advised the intravenous use of hypertonic plasma solution. I have used it with almost dramatic effect, as though a tracheotomy had been done. The administration of about 20 cc. of it intravenously to children with this condition will sometimes decrease the edema of the larynx sufficiently to allow better breathing, and a tracheotomy may not have to be done.

It is after a tracheotomy that I find most of the trouble arising because nurses are not trained in what to do with the patient. We say to them, "Do this," or "Do that," without actually showing them how to do it.

Those who do not see many children with this condition will sometimes find, to their discomfiture, that the child is apparently dead on arrival at the hospital. For such occurrences, the nurses have to be shown how to use an aspirator down through the tube. I have seen them put a suction catheter about 2 inches (5 cm.) long into the tube and think they have reached all the way down into the bronchi. They are afraid to go deeper. They have to be shown how far down into each bronchus they need to place the tube and how to turn the tube a little to reach into the various bronchi. Interns are also afraid to use a tube; they think they are going to kill the patient by inserting a rubber tube into the bronchi. I instruct each one individually.

Furthermore, one must listen to the child's chest each time one comes into the room. I never fail to listen to both sides of the chest with a stethescope each time I come into the room. One side may be atelectatic without there being much difficulty in breathing. If, by any chance, a little of that crust will go to one side, the child will die without a chance. I always make sure that both sides are open, front and back. It takes hardly any time at all.

Another thing I do, which is probably unorthodox and may or may not be acceptable to most physicians (I have been criticized, but so far nothing has happened), is use oil in the bronchi. I use the no. 30 refined peanut oil. I instil it through the tracheotomy tube exactly as is done with a saline solution, but when it gets down I have the nurse insert a fluid, and so practically nothing gets into the alveoli. The oil does, however, open up the tracheobronchial tree and soften the crusts much better than either a saline solution or a solution of sodium bicarbonate. I have never seen anything happen to the lung with the use of this oil. Like iodized oil, it should not hurt the trachea, bronchi or lungs. I have used it for several years and have never yet had to do a bronchostomy. It does not have to be used very often, perhaps two or three times a day—and just a few drops, enough to run down. I found it to be very successful. I should not suggest using so much of it that it stays down in the lung, but if it is sucked out after its use, there should be no difficulty.

Dr. John R. Simpson, Pittsburgh: The method described of humidifying the air is adequate and can be promptly installed, a minor objection being that pools of water collect on the rubber blanket.

In reply to Dr. Galloway: We have not used his method of drainage routinely. In 1 case, with some loss of use of the muscles of the chest after infantile paralysis, raising the foot of the bed facilitated the expulsion of secretions.

MODERN MANAGEMENT OF OROANTRAL FISTULA

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MANY chronic oroantral fistulas treated in the past could have been prevented had certain steps been taken immediately after their occurrence. There is a necessity for improvement in the manner in which these lesions are managed. It is the purpose, therefore, of this paper to outline those modern measures which have proved most successful in the treatment of this condition.

MATERIAL AND METHODS

In the past four years I have treated 41 patients with oroantral fistulas. Of these 12 had so-called acute fistulas and 29 had chronic fistulas. In all but 6 the condition represented the result of extraction of diseased teeth which opened the antral floor. Of these remaining 6 patients, 3 had chronic fistulas caused by a dentigerous cyst eroding into the maxillary sinus. A fourth patient was a Marine lieutenant with a single fistula which resulted from a gunshot wound received in hand to hand fighting at Okinawa, and which was similar to that in the second case reported by Wible and Howard.[1] Two perforations followed a Caldwell-Luc operation (radical maxillary sinusotomy). Eight of the patients with chronic fistulas had experienced one or more previous attempts at closure before coming under my care. The methods I have developed for the management of this condition are not original but represent a combination of the better suggestions of many authors together with the use of modern antibiotic drugs.

Acute Oroantral Fistula.—This term is used to designate those lesions in which the connection between the mouth and the antrum has been recently established. This condition is usually associated with acute or subacute maxillary sinusitis of some degree.

After a maxillary tooth has been extracted, the signs that the antrum has been entered are (1) bleeding from the nose, (2) escape of air through the socket with expiration, (3) frothing or bubbling of blood in the socket and (4) escape of liquids in the mouth through the nose.[2] If any of these signs occur, or if signs or symptoms of a general toxic state follow, the patient should have the immediate care of a rhinologist.

Presented at the Clinical Congress of the American College of Surgeons, Los Angeles, Oct. 21, 1948.

From the Department of Otolaryngology, University of Southern California School of Medicine, Los Angeles.

1. Wible, L. E., and Howard, J. C., Jr.: Traumatic Palatal Fistula, Arch. Otolaryng. **44**:159-165 (Aug.) 1946.

2. Berger, A.: Oroantral Openings and Their Surgical Corrections, Arch. Otolaryng. **30**:400-410 (Sept.) 1939.

In this series, as soon as was possible, after the signs appeared, the antrum was washed through the inferior meatus to remove blood and pus. Cultures were made if pus was obtained. Five cubic centimeters of penicillin (5,000 units per cubic centimeter of isotonic sodium chloride solution) was then instilled. Roentgenograms were always taken thereafter. In treatment, care was taken never to curet, probe or pack the socket.[3] Irrigation through the fistulous tract was always considered inadvisable. Finally, each patient was instructed to avoid blowing his nose.

The fistula was then closed by biting the alveolus away with the rongeur, if necessary, and approximating palatal and buccal mucoperiosteal flaps with mattress sutures.[4] When possible, a temporary so-called saddle plate of dental composition was made to fit snugly over the sutured area and prevent oral secretions from escaping into the antrum. This plate was designed in the manner described by Strong,[5] i. e., to lie over the sutured flaps but not in any way to extend into the fistula. The plate was held in place by wires or sutures, arranged according to the location of the fistula and the number of surrounding teeth. The patient was placed on a liquid to soft diet, and mastication was done on the opposite side of the mouth.

If the roentgenograms demonstrated a fragment of tooth or other radiopaque foreign body, the substance was removed from the antrum by a radical maxillary sinusotomy. If, on the other hand, there was evidence that the maxillary sinus had been infected previous to the formation of the fistula, an antral window was made. The sutures and saddle plate were usually taken out on the tenth day. However, some were removed sooner when it was evident that the fistula was closed.

When signs of maxillary sinusitis did not appear aften ten days of daily irrigations and instillation of penicillin, no further treatment was considered necessary. If, however, acute sinusitis developed, the instillations were continued along with intramuscular injection of penicillin until the infection was brought under control and the fistula closed. When the fistula closes only partially and continues to drain for three or four weeks, the lesion must be considered chronic and treated accordingly.

Chronic Oroantral Fistula.—This term is used to designate those lesions in which the connection between the mouth and the antrum has been long established. In such instances the tract usually has become partially or completely epithelized. The primary problem is the elimination of the sinusitis, inasmuch as it is usually the purulent drainage from the antrum that prevents the fistula from healing spontaneously. However, besides epithelization of the tract and chronic maxillary sinusitis, other factors, such as osteomyelitis of the maxilla or an unusually large bony defect, may occasionally explain the failure of these communications to close spontaneously.

In treatment of chronic oroantral fistulas, the Caldwell-Luc procedure was found to be best suited to accomplish all the necessary measures, namely, removal of the antral infection, removal of the diseased bone or foreign body, removal of the entire epithelial lining of the fistula and correction of the defect in the roof

3. Hall, S. S., and Thomas, H. V.: Maxillary Sinusitis of Dental Fracture Origin, W. Virginia M. J. **38**:146-155, 1942.

4. Cogswell, W. W.: Dental Oral Surgery, Pittsburgh, Dental Digest, Inc., 1932, p. 309.

5. Strong, C. N.: Some Considerations of the Pathology and Treatment of Dental Infections of the Antrum, Proc. Roy. Soc. Med. **29**:1547-1552, 1936.

of the mouth. Therefore, in order to secure the uniformly best results, this operation was performed and the fistulous lining removed. The defect was closed at the same time by whichever plastic procedure best suited the individual case. This was always done at the same time as the operation on the sinus in order to avoid reinfection of the antrum, although delayed flaps were occasionally employed.

The Caldwell-Luc incision was frequently included in the flap incisions and the entire wound sutured tightly, as described recently by McQuiston.[6] Care was taken to make the palatal incision medial to and parallel with the greater palatine artery and palatine nerves to preserve the blood supply of the flap. After operation, the antrum was irrigated daily and penicillin instilled thereafter. As this was done gently, and with little pressure through the inferior meatus, the clot and granulations in the fistulous tract were not disrupted. The same precautions were taken as those described for the acute condition; i. e., probing, packing, curetting and irrigating the tract were avoided, and the patient was instructed to avoid blowing his nose.

With patients requiring more extensive plastic repair, a variety of surgical technics may be used, the discussion of which is not within the scope of this paper.

TABLE 1.—*Data on 12 Cases of Acute Oroantral Fistula*

	Number of Cases
Lesion	
Simple fistula	9
Fistula with acute sinusitis	3
Location	
First molar	3
Second molar	9
Treatment	
Immediate closure, penicillin irrigations	11
Immediate closure, penicillin irrigations plus nasal antrotomy	1

Many authorities have described their own methods of plastic closure, and the subject has been well reviewed by Major.[7] Others have added new technics more recently.[8]

RESULTS

With the technic described, uniformly successful results in management of the acute fistulas were obtained in producing primary closure of the oral wound. It should be pointed out that the majority of, but by no means all, the untreated acute fistulas heal spontaneously. However, every one in this series closed, and acute maxillary sinusitis developed in only 3 patients (table 1). These patients had all consulted the rhinologist more than twenty-four hours after the extraction. Antral irrigations

6. McQuiston, R. J.: Maxillary Sinusitis of Dental Origin and the Management of Antral Fistula, Ann. Otol., Rhin. & Laryng. **54**:373-383, 1945.

7. Major, G.: Buccoantral Fistula: A Method of Closure, Arch. Otolaryng. **29**:319-325 (Feb.) 1939.

8. Proctor, B.: The Closure of Oromaxillary Fistulae—A Preliminary Report, Laryngoscope **56**:46-47, 1946. Hersh, J. H.: Plastic Repair of a Large Alveolar-Antral Fistula, Arch. Otolaryng. **43**:141-142 (Feb.) 1946. Tholen, E. F.: Closure of Oral Antral Fistula, J. Oral Surg. **3**:255-257, 1945.

TABLE 2.—*Data on 29 Cases of Chronic Oroantral Fistula*

	Number of Cases
Lesion	
Fistula with chronic sinusitis	16
Fistula with dentigerous cyst	3
Fistula following Caldwell-Luc operation	2
Fistula with foreign body in and osteomyelitis of antrum	1
Fistula with foreign body in antrum	7
Treatment	
Caldwell-Luc operation and construction of buccopalatal flap	26
Construction of inferior meatal window	3

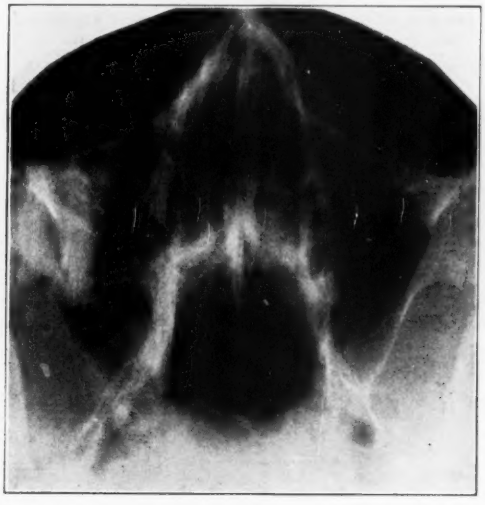

Fig. 1.—Osteomyelitis of the maxilla and oroantral fistula. A complete bony shelf dividing the antrum into two chambers was discovered at operation. The upper cavity was lined with normal mucosa and walled with normal bone. The lower cavity contained a 6 inch (15 cm.) piece of iodoform gauze, and the walls were completely absorbed by an osteomyelitic process. The gauze had been acquired during some ill advised dental treatment of the fistula.

and roentgenograms revealed evidence of inflammation at their first visit, indicating that the sinusitis had developed prior to adequate therapy. Even these patients responded satisfactorily when given immediate vigorous treatment.

In 1 case of acute fistula it was thought necessary to construct an inferior meatal window because the patient had waited six days for further consultation. The patient complained of a foul discharge from the nose and the fistula. He had no fever or headache. Washings from the maxillary sinus yielded a large amount of fetid pus. Roentgenograms made after lavage demonstrated considerable thickening of

the mucous membrane of the sinus; this thickening was interpreted as evidence of a preexisting sinusitis of subacute or chronic nature.

Treatment of the chronic fistulas resulted in failure in 3 cases. It was believed that treatment failed in 2 cases because an antral window was constructed when a Caldwell-Luc procedure was indicated, owing to chronic, irreversible changes in the mucous membrane. The window was constructed in each case because the patient refused a more radical operation. Treatment in the third case was not successful because of excessive tension on the flaps. It should be pointed out that in 8 of the 29 cases of chronic fistula there were foreign bodies in the antrum (table 2), only 3 of which could be visualized on roentgenologic examination. In 2 cases sequestrums were free in the antrum; in 1 case, iodoform gauze (fig. 1); in 2 cases, tooth fragments (fig. 2), and in 1 case each, a ball of cotton, a piece of chewing gum and a shell fragment.

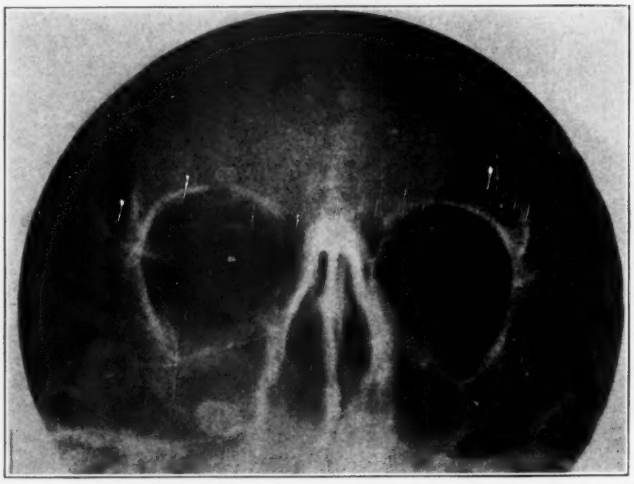

Fig. 2.—Dentigerous cyst and oroantral fistula. The cyst contained a large fragment of tooth and much fetid pus. The antrum itself, however, was lined with normal mucous membrane. Both the dentist and the previously consulted rhinologist had been puzzled because pus could not be obtained from the nose when irrigations were done through the fistula or through the natural antral ostium.

COMMENT

In following many cases of oroantral fistula, one is impressed with the lack of cooperation between the dentist or oral surgeon and the rhinologist. Yet, in reviewing the literature, one reads repeatedly the plea for better teamwork between the two specialties. This lack of

cooperation exists apparently because the dentist mistakenly feels that the fistula was the result of an operative error instead of an unavoidable accident, as is frequently the case. For this reason he is often reticent about asking for consultation. Furthermore, there is a tendency to minimize the involvement of the sinus and to attempt vainly to close the fistula without treating the sinusitis. These facts make for a greater incidence of chronic oroantral fistula.

Attention must be given to the involvement of the sinus, whether acute or chronic, or attempts at closure of the fistula will be futile. Such fistulas are primarily problems of acute or chronic sinusitis and should be seen by the rhinologist.[9] The actual closure of the fistula usually is of secondary importance to the elimination of the sinus disease.

Escharotics should be abandoned. Their use, as suggested by Weih,[10] who used trichloroacetic acid, and Drury,[11] who used "liquor epispasticus" (a 50 per cent acetic acid tincture of cantharides), rarely results in complete closure and produces so much scarring that the employment of flaps or grafts later is usually unsuccessful; yet many patients of this series came to me having been treated with silver nitrate regularly until the area surrounding the fistula consisted of the most avascular scar tissue.

In 1925 Lyons[12] recommended a treatment for acute oroantral fistulas in which the soft tissues were routinely sutured over the fistula and an antral window made. No irrigations were allowed. The present use of penicillin makes an antrotomy rarely necessary provided the patient is seen immediately. The irrigations, followed by instillations and systemic administration of penicillin, clear the acute sinusitis quickly. If lavage is done gently, it is my opinion that it does not disturb the wound. In this I differ from Hill.[13]

MacGougan[14] reported a successful result in a case of acute oroantral fistula treated by plastic closure and several irrigations of the antrum. Maxillary sinusitis had developed a few weeks after extraction of a tooth. MacGougan used a 20 per cent suspension of sulfathiazole powder in glycerin for instillation into the antrum after irrigation.

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9. Mundt, G. H., in discussion on Lawson, L. J.: Changing Concepts of Therapy of Chronic Sinusitis, Arch. Otolaryng. **46**:120 (July) 1947.

10. Weih, E. P.: Closure of Alveolar Fistula by Scar Tissue Formation, Ann. Otol., Rhin. & Laryng. **39**:533-541, 1930.

11. Drury, D. W.: A Procedure for the Cure of Antral Fistulas, Boston M. & S. J. **191**:1123-1124, 1924.

12. Lyons, H. R.: The Treatment of Alveolar Fistula Secondary to the Extraction of Teeth, Tr. Am. Laryn., Rhin. & Otol. Soc. **35**:81-88, 1929.

13. Hill, F. T.: Management of the Alveolar Fistula, Arch. Otolaryng. **40**:167-170 (Sept.) 1944.

14. MacGougan, M. K.: Maxillary Sinusitis of Dental Origins: Two Cases Treated Conservatively, J. Canad. M. Serv. **2**:579-581, 1945.

Lyons also warned against irrigating through the fistula. He opposed packing the socket; yet both these errors were committed twice by exodontists in cases in this series. Hall and Thomas warned against probing the socket; yet 1 patient in this group described the dentist's pushing the probe around in the antrum at all angles to demonstrate to the patient the size of the sinus (fig. 3), without realizing that he was succeeding only in enlarging the fistula.

In the management of chronic oroantral fistula, the question whether a radical maxillary sinusotomy is indicated is frequently debated. My experience leads me to agree with those [15] who advocate this more

Fig. 3.—Chronic maxillary sinusitis secondary to an oroantral fistula. The history was a common one, with the dentist wondering whether he had entered the antrum and then probing the socket vigorously to determine whether he had. A primary closure was obtained after a radical maxillary sinusotomy and suturing of the buccopalatal flaps.

radical procedure for uniformly good results. Endonasal operations are occasionally successful, as demonstrated in 1 of the cases in this series, but the radical technic offers a better chance of ridding the antrum of chronic disease. It also offers the surgeon a better opportunity to inspect the sinus for polypoid membrane or a foreign body, as well as

15. Strong.[5] Major.[7] Lyons.[12] MacGougan.[14] Hempstead, B. E.: Intranasal Surgical Treatment of Chronic Maxillary Sinusitis, Arch. Otolaryng. **6**:426-433 (Nov.) 1947. Ashley, R. E.: A Method of Closing Antral-Alveolar Fistulas, Ann. Otol., Rhin. & Laryng. **48**:632-642, 1939.

a more complete way of dissecting out the epithelium of the fistulous tract. Berger stated that an oroantral fistula should never be closed without careful inspection and exploration of the cavity for a foreign substance. As the object may be nonopaque to roentgen rays, only a radical maxillary sinusotomy can provide opportunity for such examination. This procedure represents little more of an ordeal to the patient than does an endonasal antrotomy.

CONCLUSIONS

1. Oroantral fistula, whether acute or chronic, is essentially a problem of sinusitis and should be managed by a rhinologist.

2. Many cases of chronic oroantral fistula or chronic suppurative sinusitis of dental origin could have been prevented had immediate vigorous therapy, such as described here, been instituted.

3. Probing, curetting, packing, irrigating or cauterizing an oroantral fistula should be strictly avoided.

4. Radical maxillary sinusotomy and Caldwell-Luc operation give the uniformly best results in treatment of chronic oroantral fistulas.

5. There is a need of more serious attention by exodontists to oroantral fistulas.

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STRUCTURE AND PERFORMANCE IN ANIMAL LANGUAGE

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YOUATT,[1] in 1835, found it hard to explain why his young chimpanzee "had not the slightest power of speech, though he could scream loudly." The fact that higher animals do not make "appropriate" use of their otherwise suitably constructed organ of voice prompted many speculations.

The conception that production of sounds and language are related to the degree of development of the brain rather than to the structure of the larynx has found numerous advocates. The origin of such statements can be traced to the sentence of Darwin, dating from 1871: "The fact of the higher apes not using their vocal organs no doubt depends on their intelligence not having been sufficiently advanced." This interpretation was extended to conditions as found in man, and so when Polyak, McHugh and Judd,[2] in 1946, wrote that "It is legitimate . . . to conclude that the cause of relatively late development of the human ability to communicate by spoken words was not the insufficiency of the sound producing and word shaping organs but the poorly developed mental sphere."

The concept of Rochon-Duvigneaud [2a] with regard to the eye and vision in monkeys is similar: namely, that they see with the same eye as man but look and observe with a much inferior brain.

Advance in the differentiation of vocal communication may even have branched off from the main phylogenetic line. Nissen [3] stated that it "may be more highly developed in some infra-primate societies [e. g. birds] than among the monkeys and apes. In chimpanzees, directive communication is largely gestural and postural. . . ."

From the Biological Laboratories, and the Department of Otolaryngology, Harvard Medical School. This study was aided by a grant from the Ella Sachs Plotz Foundation.

1. Youatt, W.: Account of the Habits and Illness of the Late Chimpanzee, Lancet 1835-1836, pp. 202-206.

2. Polyak, S. L.; McHugh, G., and Judd, D. K.: The Human Ear in Anatomical Transparencies, New York, T. H. McKenna, Inc., 1946.

2a. Rochon-Duvigneaud, A.: Les yeux et la vision des vertébrés, Paris, Masson & Cie, 1943.

3. Nissen, H. W.: Primate Mentality, in Harriman, P. L.: Encyclopedia of Psychology, New York, Philosophical Library, Inc., 1946, p. 552.

Yerkes and Learned[4] formulated the problem as follows: "Although the animals [chimpanzees] have a sound-producing apparatus which presumably is capable of functioning much as does that of man, there is slight, if any, tendency to imitate sound."

In the attempt to coordinate anatomic structure and vocal performance, two surveys have been given earlier (Kelemen[5]). One dealt with an area of special phonetic significance, the junction of the larynx and the resonant tube; the other discussed the role of respiratory voice in comparative phonetics. Both studies left the impression that conditions as found in the end organ do not justify one in expecting higher vocal achievement than that commonly observed in untrained animals. In a later report,[6] instead of tracing in a number of different species a single anatomic area or a single phonetic function, it was endeavored, rather, to study anatomy and function in a single species. Given a certain structure, the possibility of reaching a degree of phonetic performance warranted by the higher developed mental faculties was reviewed. The chimpanzee was chosen because a number of descriptions of its vocal organ are available and because there is no other animal whose vocal performance has been studied and analyzed as thoroughly and competently. It seemed advisable to attempt such a coordination because the anatomic descriptions include but few statements regarding function, and analyses of voice and speech of the chimpanzee disregard the anatomic situation. The number of animals studied in the pertinent literature is small,[5b] and such reports as are extant are inadequately supported by histologic evidence and not at all by observations of serial sections. Moreover, there is considerable variation in laryngeal musculature in anthropoids.

Continuous histologic series of the larynx, divided in midplane into a right and a left half, were examined, with one of the halves sectioned in the horizontal, the other, in the frontal, plane. Microscopic observation has shown that the opening of the aditus laryngis directly faces the posterior pharyngeal wall. [For detailed description of these series and the grouping according to cartilages, articulations, extrinsic and intrinsic ligaments, muscles and cavity of the larynx, see footnote 6.] The larynx is suspended so high that the corniculate and cuneiform cartilages reach the level of the lowest bundles of the lingual muscles.

4. Yerkes, R., and Learned, B.: Chimpanzee Intelligence and Its Vocal Expression, Baltimore, Williams & Wilkins Company, 1925.

5. (*a*) Kelemen, G.: Comparative Anatomical Studies on the Junction of Larynx and Resonant Tube, Acta oto-laryng. **26**:276-283, 1938; (*b*) Vergleichend-Anatomisches und -Physiologisches zur inspiratorischen Stimmbildung, Monatsschr. f. Ohrenh. **66**:953-963 (Aug.) 1932.

6. (*a*) Kelemen, G.: The Anatomical Basis of Phonation in the Chimpanzee, J. Morphol. **82**:229-256 (March) 1948; (*b*) Vergleichende Anatomie und Physiologie der Stimmorgane, Arch. f. Sprach- u. Stimmphysiol. **3**:213-237 (Oct.) 1939.

The full impact of respiratory air current falls on the posterior part of the glottis, while the most frontal section of the vocal cord remains tightly covered by the epiglottis. A posterior channel—hiatus intervocalis, Némai [7]—between the concavity of the cricoid cartilage and the excavated medial surface of the arytenoid cartilages, on the one side, and the vocal process of the arytenoid cartilages on the other, cannot be closed entirely. Covering like a curtain the greater lower part of the entrance to the ventricle, the vocal lip forms a transparent epithelial structure, ending in a sharp upward-turned horizontal edge. The vocal lip is attached by its entire height to the vocal process and the crista arcuata and is moved inward with the displacement of the vocal process, opening the entrance to the ventricle. The conus elasticus is strongest, smoothest and most homogeneous, coming nearest to what can be called a true vocal cord, at the level of the most prominent bulge of the thyroarytenoid muscle; this level corresponds to a level below the floor of the ventricle. An inward curve of the thyroid cartilage lends a solid base for the muscular bulge, resulting in formation of an isthmus at this level. The lateral laryngeal wall is completely pneumatized.

Rather than to add to the volume of speculations of questionable usefulness regarding function, it was preferable to sketch the limitations of phonetic production in comparison with human performance. This procedure seemed to be in accord with the postulate of Revesz,[8] who pleaded for the omission of spiritualistic hypothesis or complicated theories in psychologic investigations with animals if a simple way would be sufficient to explain occurrence and performance.

With regard to the duration of sounds, difficulty in separating the soft palate from the epiglottis accounts for the absence of long, drawn-out sounds similar to those of human production, since for such sounds a constantly open oral resonant tube is necessary.

The production of double sounds is favored by a "second glottis," placed at a different level, between the arytenoid cartilages. Intermembranous and intercartilaginous glottides do not act as a unit, as they do in man and in gibbon. The hiatus intervocalis, described by Némai,[7] is present and makes clear intonation impossible, except in piano, when only the intermembranous glottis is in action.

Inspiratory voice, in man a pathologic symptom, can originate in the chimpanzee at several levels. Except for a very short section near the commissure, the edges of the vocal cords are "indifferently" shaped against a current of air striking from the aditus or from the trachea.

7. Némai, J.: Das Stimmorgan der Primaten, Ztschr. f. Anat. u. Entwcklngs-gesch. **81**:657-672, 1926.

8. Revesz, G.: Experimental Study in Abstraction in Monkeys, J. Comp. Psychol. **5**:293-341 (Aug.) 1925.

The air sac mechanism is controlled (*a*) by contraction of the platysma and other muscles of the neck spread over the external surface of the sac; (*b*) inside the larynx, by action of a sling formed by muscular bundles branching off from the thyroarytenoid muscle, regulating the patency of the appendix, and (*c*) by a hitherto unobserved action: the closing and releasing of the lumen of the appendicular duct by pressure exerted by the muscular mass of the base of the tongue. The air sac mechanism produces sounds independently of the rhythm of respiration.

In relation to the role of the vocal lip, a transparent epithelial structure ending in a sharp upward-turned horizontal edge, sounds produced at this location by the current of air evacuated from the air sacs are neither expiratory nor inspiratory. The role of delicate membranes of birds spread over a certain space was analyzed by Rüppel.[9] Tightly stretched membranes in the bat may tend, according to Griffin,[10] toward the production of supersonic vibrations. Little was observed directly about the movements of the free vocal lip or its phonetic achievement. Some information, however, can be gathered by reports on the hearing, as sound-producing and auditory capacity are closely connected. Elder[11] found that the upper limit of hearing for the chimpanzee was superior to that of man, reaching 33,300 cycles per second. At present, a parallel between the production and perception of supersonic frequencies, in connection with the peculiar formation of the vocal lip, can be suggested only as a possibility worthy of future investigation.

To build up the elements of human voice and speech, a far reaching simplification of the end organ has had to be achieved. The emission of double sounds, the use of expiratory and inspiratory phonation, complication by sounds produced at the membranous vocal lip independently from the respiratory rhythm, must have been eliminated in the course of evolution. Their participation in the phonetic performance is not an enrichment, at least in the sense that, with a different mechanism, they make the vocal apparatus utterly unfit to duplicate production of the human voice.

In the opinion of Romer,[11a] ". . . there is no reason to assume that increasing complexity or addition of new parts are processes which have

9. Rüppel, W.: Physiologie und Akustik der Vogelstimme, J. Ornith. **81**: 433-542 (July) 1933.

10. Griffin, D. L.: How Bats Guide Their Flight by Supersonic Echoes, Am. J. Physics **12**:342-345 (Dec.) 1944.

11. Elder, J. H.: The Upper Limits of Hearing in Chimpanzee, Am. J. Physiol. **112**:109-115 (May) 1935.

11a. Romer, A. S.: Time Series and Trends in Animal Evolution, in Jepsen, G. L., and others: Genetics, Paleontology and Evolution, Princeton, N. J., Princeton University Press, 1949, pp. 103-120.

a copyright on the term evolution; simplification may equally be a change leading to survival, which is the only test of success."

It is not that the larynx of the chimpanzee has remained underdeveloped amid progressiveness of the other anatomic parts; its structure forms a basis for a remarkable vocal performance, "of an almost unbelievable amount and intensity,"[12] though within characteristic limits. On the other hand, in spite of high mental qualities, the chimpanzee is incapable of imitating human speech, since its own voice is composed of entirely different phonetic elements.

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12. Nissen, H. W.: A Field Study of the Chimpanzee: Observations of Chimpanzee Behavior and Environment in Western French Guinea, Comparative Psychology Monographs, Baltimore, Johns Hopkins Press, 1931, vol. 8, no. 1, serial no. 36.

ALLERGY AS A CAUSE OF NUCHAL MYALGIA AND ASSOCIATED HEADACHE

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INTEREST in the allergic cause of various myalgias developed as a result of clinical observations on patients undergoing individual food tests [1] for the diagnosis of specific food sensitivity. Myalgia of the cervical muscles has been repeatedly observed to follow experimental ingestion of foods or exposure to inhalants in specifically sensitized persons. The facts that these muscular symptoms may be reproduced repeatedly and at will in experimental circumstances and that such complaints may be relieved by avoidance of incriminated allergens are the basis of the thesis that such manifestations are of allergic origin.

The allergic response of skeletal musculature may be localized to regional groups of muscles, to a single muscle or, apparently, to a segment of a given muscle. In other instances the process seems to involve multiple groups of muscles, such involvement giving rise to the impression that the reaction is generalized in character.

Of the various localized reactions, involvement of the nuchal muscles is the commonest, although similar responses have been observed less frequently in the calf muscles, the hamstrings, the lower muscles of the back, the pectoral muscles, the intercostals and the rectus abdominis. This presentation will be limited to the subject of chronic nuchal myalgia. Acute myalgia, or myositis of the cervical muscles as the result of food allergy, has recently been described as acute torticollis.[2] The clinical evidence favoring the involvement of other muscle groups will be presented in another communication.[3]

Read before the Chicago Laryngological and Otological Society, Nov. 1, 1948.

This investigation was aided by a grant from Swift & Company for the study of food allergy.

1. Rinkel, H. J.: Food Allergy: II. The Technique and Clinical Application of Individual Food Test, Ann. Allergy **2**:504, 1944. Randolph, T. G., and Rawling, F. F. A.: Blood Studies in Allergy: V. Variations in Total Leucocytes Following Test Feeding of Foods; An Appraisal of the Individual Food Test, ibid. **4**:163, 1946.

2. Randolph, T. G.: Allergy as a Cause of Acute Torticollis, Proc. Central Soc. Clin. Research **21**:61, 1948; J. Lab. & Clin. Med. **33**:1614, 1948.

3. Randolph, T. G.: Allergic Myalgia, to be published.

In the absence of a satisfactory and experimentally demonstrable cause, myalgia of the posterior cervical muscles has been described by a profusion of terms. One of the first descriptions was by Valleix [4] in 1841, who referred to spontaneously recurring sieges of painful contractions of muscles of the nuchal area as cervico-occipital neuralgia and mentioned André [5] and Berard [5] as his predecessors in recognizing this syndrome. He stated that involvement was commonly unilateral; that tenderness was most pronounced in limited areas at the base of the skull, the anterior edge of the trapezius and the posterior edge of the sternocleidomastoid muscle and slightly below the middle part of the neck; that the pain in these areas was accentuated by motion of the head and sometimes radiated to the shoulder or jumped to the frontal area, and, finally, that the pain was materially relieved by immobility. He mentioned that diet, exposure to cold and menstruation were precipitating factors, although he was unaware of the cause.

Norström [6] published in 1885 a treatise on the treatment of headache by massage; this treatise consisted principally of personal cases, but others were borrowed from Henschen [7] and Wretlind.[7] He attempted to show that many cephalalgias were secondary neuralgias starting from deposits of chronic inflammation of the muscles of the neck; the deposits were most commonly localized to the insertions of the muscles but also occurred in the bodies of these muscles. In subsequent editions [8] he continued to comment on the frequency of tender nutlike indurations on the edges and in the body of the trapezius muscle and along the sternocleidomastoid muscle, occurring in association with parietal or frontal cephalalgia.

In 1911 Edinger [9] was impressed with the frequency of this clinical picture, which he referred to as indurative headache, and credited the earlier work of the Swedish investigators Henschen, Norström and Helliday for his ability to understand and to treat the condition.

Halle,[10] also in 1911, described the contracted painful muscles of the nuchal area, the contraction occurring in association with heaviness, pressure and pain in the head and, less frequently, with nausea, tinnitus

4. Valleix, F. L. I.: Traité des névralgies, ou affections douloureuses des nerfs., Paris, J. B. Baillière, 1841.

5. Cited by Valleix.[4]

6. Norström, G.: Traitement de la migraine par le massage, Paris, A. Delahaye & E. Lecrosnier, 1885.

7. Cited by Norström.[6]

8. Norström, G.: Cephalalgy and Massage, New York, G. E. Steckert, 1896; Chronic Headache and Its Treatment by Massage, ibid., 1903.

9. Edinger, L., in Church, A.: Diseases of the Nervous System in Modern Clinical Medicine, New York, D. Appleton & Co., 1911.

10. Halle, M.: Myalgien in der Ohrenheilkunde, Monatsschr. f. Ohrenh. **45**:768, 1911.

and scotoma. He noticed also the concomitant occurrence of such constitutional symptoms as morning fatigue, tachycardia, a sense of anxiety or tension and a sense of "feeling mean and generally out of sorts," and he stated that such observations were commonly made on neurasthenic types of persons, who exhibited many complaints.

Two otolaryngolists, Mithoefer [11] and Seydell,[12] are to be credited with the most complete recent description of this clinical picture. Mithoefer pointed out that in some cases hypertonicity of the muscles of the neck is not accompanied with headache, in contrast with most cases with the commoner association of head pain. He emphasized also that nodular or muscular headaches were commoner in the morning on arising, a point in keeping with their possible allergic cause, in view of the characteristic morning accentuation of symptoms in masked food allergy, as described by Rinkel [13] and confirmed by me.[14]

Seydell emphasized the marked variability in the type and localization of the head pain, the fact that nodular or spastic myalgia may or may not be accompanied with conscious pain or soreness of the cervical muscles, that most frequently the patient is unaware of any discomfort until his attention is called to it by palpation of these muscles and, finally, that the patient rarely connects his headache with the nuchal symptoms. He stated further that the patient's history usually presented evidence of vasomotor imbalance and that he frequently was found to have some sort of allergy. Seydell did not find, however, that the elimination of foods to which allergic patients are sensitive prevented or cured the condition, although he failed to state what type of diagnostic methods were employed.

The rheumatologists also deal with this condition; there is no doubt that certain cases of muscular rheumatism are identical with the previous descriptions. Comroe [15] listed the trapezius and the sternocleidomastoid muscle as those most frequently involved by the fibrositis process. He pointed out also that fibrositis of the cervical muscles has been alleged to produce severe occipital and vertical headaches, as well as acute torticollis.

In the field of neurology, Riley [16] commented on the distinct variations occurring in the localization of head pain in migraine, that painful

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11. Mithoefer, W.: Hypertonic Muscles of the Neck as a Cause of Headache, Ann. Otol., Rhin. & Laryng. **43**:67, 1934; Hypertonic Muscles of the Neck as a Cause of Headache, Tr. Am. Laryng., Rhin. & Otol. Soc. **40**:285, 1934.

12. Seydell, E. M.: Indurative or Myalgic Headache, Arch. Otolaryng. **32**:860 (Nov.) 1940.

13. Rinkel, H. J.: Food Allergy: I. The Role of Food Allergy in Internal Medicine, Ann. Allergy **2**:115, 1944. ,

14. Randolph, T. G.: Food Allergy, M. Clin. North America **32**:245, 1948.

15. Comroe, B. I.: Arthritis and Allied Conditions, ed. 3, Philadelphia, Lea & Febiger, 1944.

16. Riley, H. A.: Migraine, Bull. Neurol. Inst. New York **2**:429, 1932.

symptoms often involved the neck and shoulders and that irritative motor symptoms may present themselves as localized twitchings and fascicular and myoclonic contractions.

Other cases with these descriptive features may have been confused with certain orthopedic lesions in instances in which the evidence of structural abnormality may have been somewhat speculative. Such syndromes as cervical arthritis and periarthritis, indefinite anatomic changes in the cervical vertebrae, localized myofascial lesions, anterior scalenus syndrome, cervical rib phenomena, tenosynovitis and bursitis not associated with deposits of calcium may be mentioned in this respect.

It should be apparent that the symptoms described here have been referred to by those interested in psychosomatic disease as "tension headache," the implication being that tenseness causes the neck to be tight and results in a headache. Although it is agreed that tension is frequently a part of this clinical picture, it is to be regarded as a consequence rather than an etiologic factor. It should be pointed out that tension and "nervousness" are integral parts of the fatigue picture of allergic origin, as originally described by Rowe [17] and recently reviewed by me.[18]

Muscular aching, insomnia, depression and melancholia are integral parts of this allergic fatigue syndrome. In this connection, it is of significance that Burnett [19] in 1891 carefully differentiated melancholia from neurasthenia, or "nervous exhaustion", stating that the conditions were entirely unrelated. He asserted that insomnia and nuchalgia preceded the development of melancholia and that in the well advanced case the symptoms of insomnia, nuchalgia and melancholia constituted a diagnostic triad, which served to characterize typical cases of melancholia.

Rowe [20] in 1931 was apparently the first to regard the presence of pain in the posterior part of the neck and back as an allergic response, demonstrable after the ingestion of specific foods and relieved by avoidance of incriminated foods. He described both localized and generalized

17. (*a*) Rowe, A. H.: Food Allergy: Its Manifestations, Diagnosis and Treatment, J. A. M. A. **91**: 1623 (Nov. 24, 1928; (*b*) Gastro-Intestinal Food Allergy: A Study Based on One Hundred and Ninety-Nine Cases, J. Allergy **1**:172, 1930; (*c*) Allergic Toxemia and Migraine Due to Food Allergy, California & West. Med. **33**:785, 1930.

18. Randolph, T. G.: Fatigue and Weakness of Allergic Origin (Allergic Toxemia) to Be Differentiated from "Nervous Fatigue" or Neurasthenia, Ann. Allergy **3**:418, 1946; Allergy as a Causative Factor of Fatigue, Irritability and Behavior Problems of Children, J. Pediat. **31**:560, 1947; The Fatigue Syndrome of Allergic Origin, Mississippi Valley M. J. **70**:105, 1948.

19. Burnett, S. G.: The Diagnosis of Incipient Melancholia, New York M. J. **53**:497, 1891.

20. Rowe, A. H.: Food Allergy: Its Manifestations, Diagnosis and Treatment, with a General Discussion of Bronchial Asthma, Philadelphia, Lea & Febiger, 1931.

muscle aching as a prominent part of the syndrome which he termed allergic toxemia.[17c] Rinkel [21] in 1933 mentioned aching of the neck as a point in the prodromal state of migraine due to food allergy. Otherwise, the relation of myalgia to other muscular symptoms as a possible manifestation of food allergy has received little emphasis. The point of view presented here was reported by me in 1947,[22] and Meyer,[23] citing an illustrative case, recently reported that peculiar myalgias and arthralgias that fail to meet any category are often considered on the basis of a food allergy response.

Pulling, drawing, tightness and aching of the cervical muscles are some of the most usually encountered symptoms observed in the course of performing individual food tests for the specific diagnosis of food allergy. Technicians are trained to observe whether the patient stretches his neck as if his collar were too tight, as telltale evidence of the onset of such nuchal symptoms. (Rinkel [24] referred to this gesture as the horse collar reaction!) Simultaneously with extension and flexion of the neck and rotation of the head on the shoulders, patients generally start to massage the nap of the neck. Such nuchal symptoms are usually associated with tenderness of the involved muscles; they may or may not develop into headache. It is important to point out to those patients who do get head pain after food tests that their headaches may be of any descriptive type, including occasional headaches meeting Horton's [25] description of "histaminic cephalalgia."

Once our attention had been called to the fact that this clinical picture was a result of food allergy, my associates and I began to watch for the presence of such symptoms in cases of inhalant sensitivity. Although these symptoms are less commonly associated with inhalant allergy, we have observed identical symptoms to result from sensitivity to house dust. The syndrome of cervical myalgia has been shown to follow massive exposure to house dust on repeated occasions; in a few instances it has been observed as a part of the constitutional reaction following overdosage of house dust extract. Cervical myalgia in such patients has been relieved repeatedly and for characteristic periods of time after the administration of a correctly measured therapeutic dose of house dust extract. Furthermore, it has been noted that such symptoms recur after the termination of the period of effective-

21. Rinkel, H. J.: Some Considerations of Allergy as a Factor in Familial Recurrent Headaches, J. Allergy **4**:303, 1933.

22. Randolph, T. G.: Muscular Symptoms of Allergic Origin, Proc. Am. Federation Clin. Research **4**:19, 1948.

23. Meyer, M. G.: Nonreagenic Allergy, Ann. Allergy **6**:417, 1948.

24. Rinkel, H. J.: Personal communication to the author.

25. Horton, B. T.; McLean, A. R. and Craig, W. M.: A New Syndrome of Vascular Headache: Results of Treatment with Histamine; Preliminary Report, Proc. Staff, Meet., Mayo Clin. **14**:257, 1939.

ness of a given therapeutic dose of house dust; these recurrent symptoms have been repeatedly relieved after each subsequent correctly measured therapeutic injection. The diagnostic technics with respect to measuring the degree of dust sensitivity and the therapeutic dosage effective in relieving these symptoms were those described by Rinkel.[26]

For a period, all patients with a history of headache or various types of myalgia were subjected to a careful examination by palpation of the posterior cervical muscles at the time of their initial visits, prior to and after individual food tests and during other periods when they were free from such symptoms. Marked variations in the tonicity and tenderness of the posterior cervical muscles, particularly the trapezius, were noted. In general, there was a distinct tendency for these muscles to be hypertonic and tender to palpation when first seen, at a time when most patients were having chronic undiagnosed allergic symptoms, or after the experimental induction of acute allergic reactions, as against a distinctly lessened tonicity of these muscles and the relative absence of tenderness on palpation when allergic processes were under control. In some instances apparently normal nuchal muscles, as determined by palpation immediately prior to individual food tests, became taut and tender after the ingestion of an allergenic food which had been associated with the development of head pain. In the majority of instances the evidence of contracture, firmness, tautness and tenderness of the involved muscles was the only sign of abnormality. The delayed development of tender nodules in the involved muscles was determined in a few instances.

In some patients the complaint referable to the neck muscles was subjective only and could not be verified by palpation. Other patients denied the presence of such muscular symptoms referable to the neck; yet the typical findings were present on both inspection and palpation. In these instances it was interpreted that the patient had become so accustomed to such symptoms that they had ceased to regard them as anything abnormal.

Seydell emphasized the fact that patients usually do not complain of symptoms referable to the neck muscles, apparently regarding them as a trouble they must continue to endure. Not infrequently, patients told of their experience of reporting such symptoms to their physicians, but when they were not taken seriously, sympathetically or comprehendingly, they did not discuss this aspect of their symptoms at future visits with physicians. Many patients found that physicians usually do not have a workable approach to this type of difficulty; and, although they continued

26. Rinkel, H. J., in round table discussion on Inhalant Allergy, Southwest Allergy Forum, Houston, Texas, 1946; Whealing Response of the Skin; Clinical Application of the Whealing Response; Co-Seasonal Method of Treating Hay Fever, read before annual meeting of the American College of Allergists, April 15, 1949.

to consult with their physicians about more important medical matters, they obtained more relief from current symptoms at the hands of practitioners who treat them with massage. Exceptions to this situation are the acute cases in which tenderness and stiffness are present to such a degree that vigorous massage cannot be tolerated. Apparently, in consequence of their own experience, or perhaps from a common knowledge bearing on this point, many patients with this type of difficulty receive medical attention from both licensed physicians and healers practicing beyond the pale of organized medicine, the patients voluntarily dividing their complaints, depending on whose office they happen to be visiting.

The following clinical examples illustrate the relation of posterior cervical myalgia to headache, as an expression of the allergic reaction.

REPORT OF CASES

R. R., a woman aged 43, had been subject to perennial nasal allergy since childhood; this allergy had been most troublesome during winter months, and individual attacks of sneezing and rhinorrhea had been known to follow exposure to dust. Intermittent abdominal cramps and diarrhea had also been present since childhood; in more recent years, gastrointestinal attacks had followed the ingestion of milk, crab, lobster and shrimp.

For the past seventeen years, the patient had complained of attacks of pulling, drawing and tightness of the posterior cervical muscles. These symptoms sometimes occurred without associated headaches, but more frequently, generalized headaches were preceded by tautness and stiffness of the nuchal muscles. During the winter before her initial visit, stiffness of the neck and shoulders had been present continuously, being particularly troublesome on arising in the morning. Pain in the shoulder and neck usually radiated upward to the cranial attachments of the cervical muscles, but at times also radiated into the shoulder areas. She had also been subject to intermittent bouts of urticaria and a chronic degree of fatigue for the past decade. The fatigue was accentuated during winter months and had been materially relieved while she lived in the South.

The patient had been in good health otherwise except for occasional attacks of sacroiliac pain, the first attack coming on after she strained in opening a window.

On allergic investigation, it was found that she was sensitive to dust, but there was no other evidence of inhalant sensitization. Treatment with house dust during the past winter has been effective in completely relieving the symptoms referable to the neck and associated headaches. She obtains approximately ten days of relief from the muscular symptoms and headaches after each dust treatment and notices the recurrence of fatigue and cervical myalgia from between ten and twelve days after each dust injection. A longer interval between injections is followed by recurrence of the headaches.

By avoiding milk and incriminated sea foods, she has not had any recurrence of gastrointestinal symptoms. The inadvertent or experimental ingestion of these foods has been followed by sharp gastrointestinal reactions. The avoidance of eggs and chocolate has controlled the urticaria. The ingestion of either has been shown to precipitate urticaria or pronounced edematous reactions of the orbital structures.

D. S., a housewife aged 32, had had recurrent headaches since the age of 16. The onset of individual attacks was characterized by an initial sense of tenseness at the nape of the neck, followed by progressive drawing and tautness of the posterior cervical muscles. Aching pain at the base of the skull gradually extended over the head to the frontal area bilaterally. In some attacks the muscle tightness spread over the shoulders and the upper part of the back. The headaches were occasionally associated with dizziness and nausea, but there were no other gastrointestinal or neurologic manifestations. At times, particularly in recent years, she has had continuous headaches for periods of several days or weeks, during which she complained of constant aching and stiffness of the nuchal muscles, as well as of tenseness and drawing of the muscles of the lower part of the back, although repeated roentgenograms of the spine did not reveal any structural abnormality to account for these symptoms. Some transitory relief from the muscular symptoms was obtained by massage.

The patient has also been subject to chronic fatigue, which at first was present intermittently, but which has been a constant symptom during the past three years. The fatigue was characteristically accentuated in the mornings, present to a greater extent on certain days than on others, not relieved by an excessive amount of sleep and, at times, interfered materially with her daily work. She had periods of extremely troublesome insomnia. At times she was unable to fall asleep, and at other times she awakened in the middle of the night and was unable to return to sleep. She commonly awakened with a violent nightmare.

Intermittent mild nasal stuffiness had been present for several years but had never been a major symptom. The patient stated that ingestion of members of the cabbage family caused gastrointestinal symptoms, but she suspected no other foods.

A diagnosis of brucellosis (undulant fever) had been entertained on several occasions but had never been established. Treatment with thyroid failed to alter the course of the chronic fatigue or other symptoms. Repeated physical examinations did not reveal any abnormality to explain the numerous symptoms. There was no evidence of inhalant sensitivity either from the history or from skin tests with inhalants.

An individual food test with wheat was followed by a violent migraine type of headache, which began with the customary pulling and tautness of the posterior neck muscles. A similar test with corn was associated with recurrence of myalgia of the shoulders and slight nasal stuffiness. A test with potatoes was followed by intense itching of the ears, mild rhinitis and recurrence of insomnia the night after the test. The experimental feeding of eggs was associated with the development of fatigue, excessive belching and recurrence of the aching type of pain across the shoulders and the posterior portion of the neck. Sensitivity to grapefruit was determined from food diary evidence, in that each meal in which it had been eaten was followed by abdominal cramps.

By avoiding the incriminated foods, the patient has had complete relief from headaches, fatigue, insomnia, nightmares and the muscular symptoms referable to the posterior portion of the neck and the lower part of the back. On repeated occasions, the deliberate or inadvertent ingestion of wheat, potatoes or eggs has resulted in the recurrence of these symptoms.

A. G., a dentist aged 48, had been subject to periodic sick headaches since 1928. These attacks had been occurring with increasing frequency for the past eight years, and immediately prior to his initial visit in the spring of 1947, he had been awakening with a low grade headache.

Individual seizures of migraine usually began with a drawing sensation, tautness and aching pain in the left posterior cervical muscles, which, in the course of three or four hours, would be followed by severe occipital or frontal pain on the left. Less frequently, the head pain started in the frontal or occipital areas and subsequently involved the nuchal muscles. During the severer bouts, he usually had associated photophobia, blurring of vision, scotomas, hoarseness and thickness of speech, and he complained of exhaustion, impairment of memory and inability to concentrate.

Not infrequently, he would awaken with soreness and tenseness of the trapezius muscles and the muscles in the small of the back. Approximately twice yearly on the average, he was awakened during the night or in the morning with acute wryneck; this was characterized by exquisite pain and tenderness sharply localized to the superior fibers of the belly of the trapezius muscle, pronounced spasm of the affected muscle and such extreme pain on motion of the head as to immobilize the head and shoulders.

Unrelated to the headaches were intermittent, sharp transitory chest pains; these occurred most commonly in the left side of the chest and seemed to be localized to the superficial musculature of the chest. These pains did not radiate in any characteristic manner and were unaffected by respiratory movements.

In addition, the patient had been subject to perennial nasal allergy for several years; this was characterized by morning accentuation of nasal obstruction, an increase of postnasal mucus and a hacking type of cough. He also had intermittent bouts of sneezing at any time of the day. Any type of alcoholic beverage precipitated a headache, and at times the patient suspected also milk, orange and peanuts of bringing on an attack of head pain.

Repeated physical examinations and electrocardiograms did not indicate any significant abnormality. There was no evidence of inhalant allergy, and cutaneous and intracutaneous tests with inhalants gave negative results. An individual food test with milk was associated with the development of somnolence ten minutes after the initial experimental feeding. A second feeding of milk was followed within a few minutes by extreme fatigue and an unmistakable accentuation of the rhinitis. The patient had a severe headache on awakening the following morning. A similar test with corn produced decided weakness and "trembling" sensations, beginning one-half hour after the second feeding; these were followed in an hour by a headache of such severity as to require ergotamine for symptomatic relief. An individual food test with eggs was associated with pronounced leukopenia in the absence of reactive symptoms. Similar tests with wheat and potatoes did not produce any symptoms.

On the third day of a diet omitting milk, corn and the suspected foods, orange and peanuts, he noticed a striking relief from the headaches and related muscular symptoms. Sensitivity to rice was suspected on the basis of food diary evidence and confirmed by an individual food test. With the elimination of these incriminated foods, the patient reported that he was able to accomplish twice as much work, was much less irritable and was able to think better.

During the past year he has found that grapefruit produced these symptoms, and he now finds that eggs and pork are not tolerated in successive feedings but may usually be rotated in the diet. On different occasions, the ingestion of small amounts of corn sugar has resulted in the precipitation of headaches. By avoiding the major offending foods and by spaced feedings of several other foods to which he is less sensitive, he had remained free from troublesome headaches and myalgia. In view of the widespread nature of food reactions, it has not been possible to afford him complete relief from symptoms, but he estimates that he has improved approximately 80 per cent.

H. H., a social worker aged 59, had had intermittent headaches for fifteen years. Individual attacks usually began with sensations of tightness and drawing of the posterior cervical muscles and were followed by the development of generalized head pain, usually associated with scotomas and nausea. In recent years she experienced a persistent tightness and stiffness of the posterior cervical muscles occurring between the episodes of head pain. These symptoms had been so troublesome that she sought the regular services of a masseur.

For a year prior to her initial visit in the spring of 1947, she had had persistent rhinitis with superimposed attacks of acute nasal obstruction, each attack lasting two or three days. Chronic fatigue, unrelieved by a customary, or even an excessive, amount of rest, had also been present for the same period. In addition, the patient complained of occasional unexplained attacks of abdominal cramps, associated with loose stools containing copious amounts of mucus. She knew that exposure to house dust accentuated the nasal symptoms but did not suspect items of diet to be the precipitating factors.

Except for typical morphologic changes in the nasal mucous membranes, and tenderness, increased tonicity and "doughiness" on palpation of the posterior cervical muscles, the physical examination showed no abnormalities. On allergic investigation, it was found that the patient reacted positively to house dust but reacted negatively to other inhalant allergens.

An individual food test with corn was associated with the development of somnolence and rhinitis thirty minutes after the initial feeding, followed shortly by the coincident development of a severe generalized headache and a sense of increased pulling and drawing of the posterior cervical muscles. These symptoms persisted for twenty-four hours after the test, as contrasted with the absence of such symptoms prior to the test feeding, except for the usual degree of chronic cervical myalgia. The headache and symptoms referable to the neck were so troublesome after the corn test that the following day she consulted her masseur, who reported that the posterior cervical muscles and muscles of the back were strikingly tighter and more spastic than on numerous previous examinations.

The milk test produced a sense of chilliness which began five minutes after the experimental ingestion of the milk and which was followed four hours later by colicky cramps and diarrheic stool. Similar tests with wheat and potatoes were not followed by an accentuation of sypmtoms.

The initial diagnostic diet eliminated corn, milk and other foods of high dietary incidence which had not been subjected to individual testing. On the third day of this diet, the patient reported considerable improvement in the degree of chronic fatigue and muscle stiffness. The untested foods were then returned to this diet and tolerated, with the exception that the cumulative ingestion of both orange and eggs was followed by recurrence of myalgia and headache.

With the avoidance of corn and milk, the use of all other foods on a rotating, diversified schedule and the continuation of specific dust therapy, she reported a pronounced improvement generally: the fatigue and rhinitis were no longer present; there were no troublesome headaches, and the myalgia was greatly improved. Her masseur reported that the posterior cervical and lumbar muscles were much less tight and "gummy." The patient observed that she was able to move her head through a greater range of motion than previously and was free from the chronic stiffness that had formerly characterized the posterior cervical musculature.

On repeated occasions the ingestion of small amounts of milk or corn, particularly in the form of corn sugar, was effective in reproducing the former symptoms. Her only severe headaches were invariably related to breaks in her diet, particularly with respect to the inadvertent ingestion of corn products.

G. H., a physician aged 44, had been subject to infantile eczema between the ages of 1 and 12 years; chronic perennial nasal allergy since early childhood; seasonal ragweed hay fever of three years' duration; intermittent episodes of perennial asthma since 1933, which were accentuated during the hay fever season in recent years, and, finally, bouts of hemicrania, associated with cervical myalgia of five years' duration, attacks of which had occurred with increasing frequency and severity during the past two years.

The individual attacks of head and neck pain were characterized by the gradual onset of mild head pain on the right frontal area, which gradually increased in severity and spread over the entire lower right side of the head becoming, at the end of three or four hours, most intense at the points of cranial attachment of the right posterior cervical muscles. At this stage the pain was intense and pulsating and was exaggerated by changes in posture, particularly on bending forward or on attempting to arise from the sitting to the erect position.

Individual attacks developed at any time of the day; they persisted from one to three days each and were not associated with any visual, neurologic or gastrointestinal symptoms. Pressure over the nuchal attachments on the right was effective in relieving these attacks only while the pressure was maintained. Although these episodes were not incapacitating, the patient was more irritable during the attacks and found it more difficult to carry on with his daily routine than when free from them.

For a number of years he had been prone to pyrosis, excessive gas, flatus and bloating. In addition, he had been subject to fascicular contractions, involving the deltoid, pectoral and orbital muscle groups and occurring without associated headache or other allergic symptoms, but gradually increasing in frequency during the past five years. He stated that during this time, on attempting to arise from a sitting position, he experienced tautness and stiffness of the hamstring and calf muscles of both legs, which were relieved after ten or twelve steps. At one time, for three months, he experienced tenderness of the right achilles tendon, present only on extension of the foot, with the consequent stretching of this tendon. At another time, for several months, he had an acute pain in the right shoulder on attempts to extend the arm above the shoulder.

For the past twenty years, the patient had been subject to chronic tiredness, worse on certain days than on others, but unrelated to the amount of sleep or rest obtained. This fatigue had been associated with difficulty in concentrating, which materially interfered with his ability to read comprehendingly. Although these symptoms were present to some extent at all times, they were commonly accentuated for two or three hours after the noon meal and on arising in the morning. For several years he had been regarded by his associates as unfriendly and reserved and had had unexplained periods of mild depression and melancholia.

At no time on examination was tenderness elicited or were nodules observed at the points of cranial attachment of the cervical muscles, and no other physical abnormalities could be detected. The clinical evidence of sensitivity to dust, feathers and silk was confirmed by positive reactions to skin tests with these materials. There were also positive reactions to skin tests with other inhalants, namely, ragweed pollen and orris root, although there was no current evidence of specific intolerance to these agents.

Avoidance of and specific therapy with house dust, feathers and silk aided in relieving the respiratory symptoms, but did not bring about a satisfactory degree of relief and did not alter the course of the other allergic symptoms.

Diagnostic studies were then undertaken for the detection of food sensitivity. Fifteen minutes after an individual food test with wheat, the patient complained

of excessive gas and bloating; these were followed by a sensation of light-headedness, giddiness and mental confusion. One-half hour after the second feeding of wheat, nasal congestion, sneezing and coughing occurred and persisted for the following twenty-four hours. He reacted compatibly to the experimental ingestion of many other major foods.

With the maintenance of inhalant therapy and the complete avoidance of wheat, there have been no unexplained recurrences of the rhinitis, asthma, gastrointestinal symptoms and localized or generalized muscular symptoms. The experimental or inadvertent ingestion of wheat reproduced the respiratory symptoms on several occasions. The symptoms of the fatigue syndrome have been completely relieved, and the patient has had only one unexplained mild headache. There has been a tremendous improvement in his sense of well-being, sociability and general outlook on life.

COMMENT

In view of the incidence with which the complaint of stiffness and aching of the posterior cervical muscles is encountered in allergic persons, both with and without associated head pain, and the frequency with which this disorder may be induced in the practice of allergy during diagnostic experimental food tests, it is surprising that it has not received greater emphasis as an allergic manifestation. Although first described in this connection by Rowe [17a] approximately twenty years ago, the allergic interpretation has actually received but meager confirmation. Instead, these symptoms seem to be considered most frequently as a so-called psychosomatic expression or as a manifestation of the rheumatic state under the descriptive term of "fibrositis."

Pulling, drawing and tautness of the posterior cervical muscles have long been regarded as a functional disturbance, and when they occur in association with head pain, the clinical picture is most commonly referred to as "tension headache"; this term carries the implication that the tense nuchal muscles are the cause of the associated headache. Although it is true that these symptoms usually occur in a sequential order, as superficially to suggest such a cause and effect relationship, the fact remains that in many persons identical muscular symptoms and headache begin simultaneously, or the onset of the cephalalgia actually precedes the onset of the myalgia. These commonly occurring types were illustrated in the case reports. Furthermore, individual cases have been observed in which on one occasion the myalgia might precede the cephalalgia, and on another the myalgia might follow the head pain; and at other times either the nuchal symptoms or the symptoms referable to the head might be the sole manifestation of an intermittent attack. In view of these common observations and the fact that I have never been able to reproduce experimentally the clinical features of nuchal myalgia in patients with such symptoms but who previously had been given the diagnosis of an allergic condition and treated for it and subsequently exposed intentionally or inadvertently to tension-producing or emotional experiences of the

type alleged to act in a causative manner, I am convinced that there must be some other underlying cause of both the myalgia and the headache.

It should be emphasized that the term fibrositis is a descriptive designation, carrying little meaning so far as etiologic factors are concerned. Even attempts to find an explanation of the pathogenesis of fibrositis, from the standpoint of careful examination of the cervical muscles involved in the fibrositis process, have met with variable results.[27]

Designations of "tension headaches," typical migraine or "fibrositis" of the neck muscles are examples of the profuse confusion and speculation with respect to the clinical evaluation of localized pain and aching sensations affecting the lower portion of the occiput, the neck, upper part of the back and the shoulders.

Attempts to differentiate such descriptive entities are rendered even more difficult, in view of the fact that one patient not uncommonly has several kinds of myalgia and cephalalgia. Actually, little is gained by such pedantics, so far as helping the patient is concerned; the use of such terms generally results in a process of pigeonholing and forgetting on the part of the physician and the seeking of other advice on the part of the patient.

Inasmuch as medical terminology is moving away from descriptive diagnosis of this type and toward diagnoses which carry an etiologic connotation, it appears advisable to discard such poorly defined designations in favor of an etiologic nomenclature whenever it can be established.

No claim is made that all symptoms of the type described here are of allergic origin, and not every condition with such associated symptoms can be specifically diagnosed and relieved as a result of allergic management. The fact remains that these symptoms may be experimentally and repeatedly reproduced in certain persons by an overdose of house dust therapy, in specifically sensitized persons by massive exposure to house dust and in food-sensitive persons by the intentional or accidental ingestion of specific food. It would seem preferable to designate cases in which this cause and effect relation may be repeatedly demonstrated as instances of allergic myalgia or allergic headache associated with nuchal myalgia, and other cases as headache or cervical myalgia of undetermined cause, until a satisfactory relation between cause and effect may be experimentally demonstrated.

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SUMMARY

Myalgia of the posterior cervical muscles has been considered in the past under a profusion of descriptive terms, in the absence of any clear conception of an underlying cause.

The clinical syndrome characterized by pulling, drawing, aching, tautness, stiffness and decreased mobility of the nuchal muscles, with and without associated head pain, has been observed, in the absence of any structural abnormalities, as an allergic manifestation, confirming the early observations of Rowe. Specific inhalants (house dust) and foods have been incriminated as causative agents, as evidenced by their ability to reproduce the syndrome in certain patients, either by exposure to house dust or by an overdose of house dust extract in specifically sensitized patients, or as a result of the test ingestion of inadvertent ingestion of foods in food-sensitive patients. Avoidance of dust by and specific therapy of the dust-sensitive patient and avoidance of known food allergens by the food-sensitive patient have resulted in relief from symptoms of this type.

Involvement of the neck muscles is the most frequently encountered manifestation of allergy affecting the skeletal musculature, although the process may localize in various other muscles or give rise to more generalized muscular symptoms.

In the cases studied, no support could be demonstrated for the theory that such clinical symptoms are manifestations of "nervousness" or psychosomatic disturbances. The term "tension headache" is believed to be a misnomer, so far as it carries any etiologic connotation.

PROBLEM OF SO-CALLED CONGENITAL ATRESIA OF THE EAR

Histologic Report of a New Case

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THE TERM "congenital atresia" is used to designate a group of relatively frequent unilateral or bilateral malformations of the external and middle ear and, in some instances, also of the inner ear. These malformations are more or less independent of one another in their manner of development but may be combined and coordinated in different ways. Atresia of the external meatus, the malformation from which the whole complex derives its name, is present in the majority of cases but not always so. In some instances the meatus is only partially missing or hypoplastic, and in very rare instances entirely normal. It seems startling at first that such cases should also be contained in this group, but it becomes understandable if one realizes that originally the atresia was believed to represent a well defined malformation. Later, however, it became clear that the atresia is only one of a whole group of malformations affecting the derivatives of the posterior ends of the first and second branchial arches. It was then realized that there is no essential genetic difference between cases with and without atresia. As a matter of expediency, the familiar and already accepted term "congenital atresia" was applied to the whole complex.

In spite of the relative frequency of these malformations and their considerable practical importance, only a limited number of cases have so far been examined anatomically or histologically. In many of them the examination was not complete enough or the report not sufficiently clear to permit a genetic analysis. A thorough knowledge of the complicated development and the intricate structure of the ear is an essential prerequisite for the study and proper description of these cases. This might explain the unsatisfactory character of many of the available reports.

In these circumstances every new case which is thoroughly described and analyzed is a valuable contribution to our still incomplete knowledge of this subject.

This work was supported by grants from the Research Council of the American Otological Society and the Hayden-Coakley Fund.

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REPORT OF A CASE

A girl, born at approximately the normal termination of an undisturbed pregnancy, died after two days (Dec. 30, 1946). Nothing is known about malformations in the family.

The postmortem examination disclosed multiple malformations (heart with transposition of the great vessels, right-sided hydroureter and hydronephrosis, cystic fibrosis of the pancreas and others).

The head showed normal configuration. The right auricle was normal; the left auricle occupied its normal position but was slightly smaller and was malformed. The helix was poorly developed, the anthelix prominent and the tragus rudimentary; immediately in front of it, there was a small appendage. The external auditory meatus was completely absent. There was bilateral cleft palate, extending anteriorly to within 7 mm. of the anterior margin of the premaxilla. The upper lip showed normal configuration. Otherwise the throat and nasopharynx appeared normal. Both tubal openings were at the normal place. Cross sections through the cartilaginous tubes showed the cartilage present on both sides and the lumen of normal width.

Histologic Examination of the Temporal Bones.—Left Temporal Bone (vertical serial sections): External Ear. The folds and hillocks which composed the malformed auricle consisted of connective and fat tissue. The auricular cartilage was rudimentary and situated in the deeper parts, showing a complicated configuration with numerous excrescences on which bundles of striated muscles were inserted. It did not extend into the folds and hillocks.

The external auditory meatus was absent, and its place was taken by connective and fat tissue.

The parotid gland was not found in its usual place.

Middle Ear. The osseous part of the eustachian tube had a narrow lumen but normal structure.

The tympanic cavity had a greatest length of 11 mm., height of 10 mm. and width of 5 mm. The lumen was very well developed considering the age, measuring 10 by 8 by 4 mm. The window niches were already free; the epitympanic space and some niches in the walls were still filled with myxomatous tissue. The antrum contained myxomatous tissue into which a small recessus of the lumen of the middle ear extended.

Anteriorly, the lower part of the tympanic cavity went over into the eustachian tube, the upper part into a wide anterior recessus (fig. 1) which extended for about 3 mm. forward. Posteriorly, the upper part of the lumen extended into the antrum; the lower part continued along the floor backward beyond the level of the ampulla of the posterior vertical canal (figs. 4 to 7).

The lumen of the tube was lined with pseudostratified ciliated columnar epithelium. The same epithelium also covered the lower parts of the tympanum throughout almost its entire length. The other parts were lined with high cuboidal epithelium. The mucosa showed normal structure; there was evidence of a fresh purulent infection with exudate in the lumen.

Osseous Walls.—In the lateral wall the tympanic bone and the tympanic membrane were missing. The resulting defect was partially filled out through a downward extension of the squama which is more marked in the posterior parts than in the other parts (figs. 5 and 7). In addition, a bony lamella in the posterior parts extended upward from the lateral part of the floor of the middle ear (figs. 3 to 7). Behind the place where the facial nerve left the middle ear, the squama met the lower lamella and fused extensively with it as well as farther

backward, where it fused with the small petrosal portion of the mastoid process. An ovoid-shaped area with an approximate length of 6 mm. and height of 5 mm. remained; it was filled out with strands of dense connective tissue (fig. 4).

It might be mentioned here that the zygomatic process of the squama and the glenoid fossa were well developed. The latter was formed entirely by the squama. The mandibular joint and the mandible showed normal configuration.

The anterior part of the squama was rudimentary; its place was taken by a backward extension of the greater wing of the sphenoid bone which extended

Fig. 1.—Section through the osseous part of the tube. The abbreviation *a, c. i.* indicates internal carotid artery; *a. m. sph.*, greater wing of the sphenoid; *ch. t.*, chorda tympani; *m. a.*, accessory muscle in tegmen; *m. t. t.*, tensor tympani muscle; *r. a.*, anterior recessus of the middle ear; *s. p. squ.*, petrosquamous sinus; *squ. t.*, temporal squama, and *te.*, tegmen.

backward to the antral region. The upper half of the anterior part of the squama lay on the outer surface of the greater wing and was separated from the latter by a thin layer of dense connective tissue (figs. 1 to 7). It was only behind the posterior end of the greater wing of the sphenoid that the squama actually formed a part of the lateral wall of the skull.

The tegmen was somewhat narrower and thicker than normal, at least in the anterior part. It took its origin from a somewhat lower point of the labyrinthine

capsule than normal and extended from its point of origin in a caudolateral direction and terminated laterally with two lips, the upper thicker and the lower thinner (fig. 2). Both of these bordered on the medial surface of the squama; the inferior

Fig. 2.—Section through the anteriormost part of the middle ear. The abbreviation *a. m. sph.* indicates greater wing of the sphenoid; *ch. t.*, chorda tympani; *m. t. t.*, tensor tympani muscle in the canal of the lower lip of tegmen; *p. st.*, styloid process; *s. p. squ.*, petrosquamous sinus; *squ. t.*, temporal squama; *t. m. a.*, tendon of the accessory muscle, inserting in a groove in the upper lip of the tegmen, and *te.*, tegmen.

lip was fused with the latter in many places. The lower end of the greater wing of the sphenoid bone in the anterior part was a short distance from the lateral

end of the upper lip of the tegmen. In the posterior part, on the other hand, they bordered on each other without, however, fusing at any place. The lower lip of the tegmen terminated in its anterior part in a longer lateral and a shorter medial lamella. In this way a semicanal with an opening directed downward was formed which contained the posterior part of the belly and the tendon of the

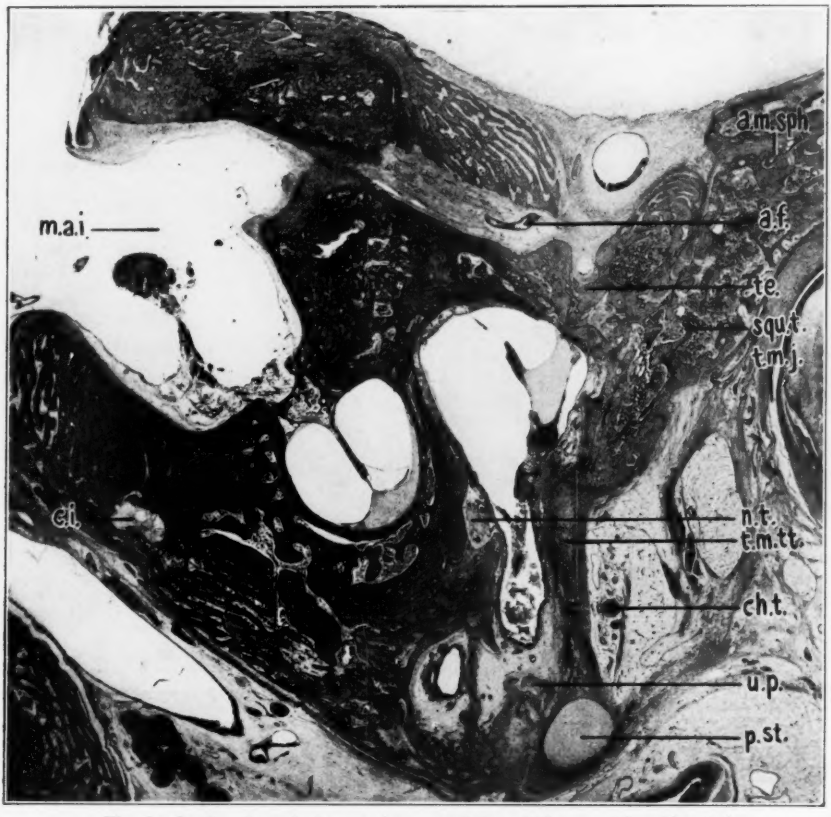

Fig. 3.—Section through the anterior part of the middle ear. The abbreviation *a. f.* indicates a branch of the internal auditory artery accompanying the facial nerve; *a. m. sph.*, greater wing of the sphenoid; *c. i.*, cartilage island in the endochondral labyrinthine capsule; *ch. t.*, chorda tympani; *m. a. i.*, internal auditory meatus; *n. t.*, tympanic nerve; *p. st.*, styloid process; *squ. t.*, temporal squama, extensively fused with the lower lip of the tegmen; *t. m. j.*, temporomandibular joint; *t. m. t. t.*, tendon of the tensor tympani muscle; *te.*, tegmen, and *u. p.*, upward process from the floor of the middle ear.

hypoplastic tensor tympani muscle (fig. 2). Between the anterior part of the upper lip of the tegmen and the medial ends of the greater wing of the sphenoid bone

and the squama, there was a deep groove which contained an anomalous muscle embedded in fibrous tissue (fig. 1). The latter was about 3 mm. long and 0.75 mm. thick and consisted of striated muscle fibers. It originated with a short tendon from the periosteum of the tegmen and of the greater wing of the sphenoid bone at approximately the level of the foramen ovale. Posteriorly its insertion was a somewhat longer tendon in the periosteum of a groove which

Fig. 4.—Section through the windows. The abbreviation *a. m. sph.* indicates greater wing of the sphenoid; *b. v. j.*, bulb of the jugular vein; *ch. t.*, chorda tympani; *d.*, defect in the lateral wall filled with strands of dense connective tissue; *l. r.*, lower recessus of the tympanic cavity; *n. VII.*, facial nerve with concomitant artery in the tegmen; *p. st.*, styloid process going over into the malformed outer ossicle; *r. w. n.*, round window niche; *s. p. squ.*, petrosquamous sinus; *squ. t.*, temporal squama; *st.*, stapes, and *t. m. t. t.*, tendon of the tensor tympani muscle inserting at the bony process extending upward from the floor.

was formed between the main part of the upper lip of the tegmen and a bony process originating from the latter and extending in a mediolateral direction over the tendon (fig. 2). The muscle received its innervation from a branch of the third division of the trimeginal nerve.

The floor was formed by a bony lamella of the os petrosum which originates from the labyrinthine capsule. It was thicker in the anterior portion and thinner in the posterior part.

On the medial wall the promontory and the window niches showed normal configuration. The fissura ante fenestram was well developed; of the fossula post fenestram, there were only traces present. A few bony bridges extended from the lower part of the promontory across the lumen to the lateral wall.

Styloid Process and Ossicles.—The styloid process, with the exception of its uppermost part, was still cartilaginous. Its lower part showed the usual course. It had a diameter of 0.75 mm. which toward the upper end increased to about 1.25 mm. The upper part of the styloid lay on the lateral surface of the bony lamella which formed the floor of the middle ear. At the posteroinferior margin of the defect in the osseous lateral wall, approximately at the level of the subiculum promontorii, it turned from its backward and upward course, upward and slightly forward, traversed the defect in the bony wall, came very near to the inferior margin of the squama, then turned slightly medially and eventually reached into the malformed ossicle (fig. 4). At the place where the styloid changed its course, a process which is 1 mm. thick continued in the original direction for 1.5 mm. and ended a short distance behind and below the place where the facial nerve leaves the middle ear. It was surrounded by a thin layer of bone from the lateral part of the floor of the middle ear (fig. 5).

The malformed ossicle consisted of a main part or body and two processes. The body lay in the epitympanic space, and, while a part of its anteromedial surface was very close to the tegmen, it did not fuse with it. The styloid process went over into the anteromedial part of the body. One of the two processes extended in a medial direction across the lumen of the middle ear to the medial wall and was here fused with the bony wall of the facial canal (fig. 5), while the other process went backward into the antrum and was connected to its lateral wall by dense connective tissue fibers (fig. 7). There was no connection between this ossicle and the stapes. The ossicle, with the exception of small areas on its surface, was completely ossified. At the point of its junction with the styloid process, the ossification could be seen progressing into the upper end of the latter process.

The stapes and the annular ligament showed an approximately normal configuration. The capitulum was covered with a thin layer of cartilage, with the exception of a small area in its upper circumference, from which a thin and short bony bridge ran to the inferolateral part of the circumference of the osseous facial canal. In this way an osseous ankylosis of the stapes was brought about (fig. 6).

Muscles.—The tensor tympani muscle was noticeably hypoplastic and was displaced laterally. In the osseous tube its belly lay near the superolateral circumference of the lumen (fig. 1) and farther backward in the semicanal formed by the lateral end of the lower lip of the tegmen (fig. 2), which has already been described. Its tendon was split into two parts, one of which inserted at the body of the malformed outer ossicle at the place where it was fused with the upper end of the styloid process; the outer part inserted at the upper end of a bony process which extended from the floor of the middle ear upward along the medial circumference of the styloid (fig. 4). The muscle was, as usual,

innervated by a branch of the third division of the trigeminal nerve. The anomalous muscle in the anterior part of the tegmen, innervated from the same source, has already been described.

The stapedial muscle was well developed and inserted at the usual place.

Fig. 5.—Section through the point of exit of the facial nerve. The abbreviation *a. m. sph.* indicates greater wing of the sphenoid; *b. v. j.*, bulb of the jugular vein; *l. r.*, lower recessus of the tympanic cavity; *n. VII.*, facial nerve; *p. o.*, medial process of the outer ossicle fused with the wall of the facial canal; *p. st.*, styloid process; *s. p. squ.*, petrosquamous sinus; *squ. t.*, temporal squama extending far downward, and *u. p.*, upward process from the floor of the middle ear.

Nerves.—The facial nerve showed a normal course within the internal auditory meatus and up to the geniculate ganglion; from the ganglion the greater superficial

petrosal nerve went off forward. The facial nerve itself turned backward and was enclosed in the tegmen for a short distance (fig. 4). The tegmen, as has already been mentioned, showed an abnormally deep origin from the lateral labyrinthine wall, going off just above the niche of the oval window. The facial nerve then entered the middle ear and lay for a short distance in an osseous canal on the under surface of the tegmen near its point of origin (figs. 5 and 6). The nerve then, instead of going downward and backward over the postero-superior circumference of the oval window frame, turned downward and laterally.

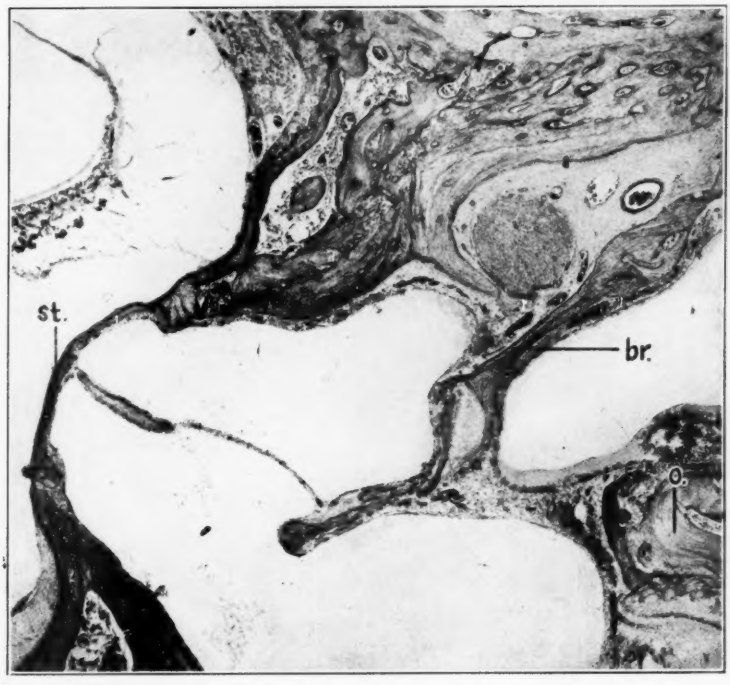

Fig. 6.—Osseous bridge (*br.*) between the capitulum of the stapes and the facial canal; *o.* indicates the outer ossicle and *st.* the stapedial footplate.

It was partially enclosed, running in an incomplete bony canal on the crest of a bony ridge which originated from the posterior part of the petrosum. The ridge extended from this point in an oblique direction anteromedially from the lateral to the medial wall of the middle ear and divided it into two parts: a supero-lateral compartment, which contained the antrum, and an inferomedial one, which contained the posterior recessus of the lumen of the middle ear, which has already been described. The nerve left the middle ear at a point which was farther forward and higher than usual. There it lay above the posterior precessus of the styloid (fig. 5). Immediately after leaving the middle ear, the facial nerve gave off

the chorda tympani and then ramified in the usual way. The chorda tympani ran forward on the lateral side of the upper part of the styloid and eventually joined the lingual nerve (fig. 1 to 4).

The tympanic nerve originated, as usual, from the glossopharyngeal nerve, penetrated the floor of the middle ear and formed a plexus (fig. 3) over the promontory which was connected with the carotid plexus through two branches. The lesser superficial petrosal nerve was missing.

Fig. 7.—Section through the facial nerve crossing the middle ear on the crest of a bony ridge. The abbreviation *a. m. sph.* indicates the greater wing of the sphenoid; *a. st. m.*, stylomastoid artery; *l. r.*, lower recessus of tympanic cavity; *n. VII.*, facial nerve; *p. o.*, posterior process of the outer ossicle; *s. p. squ.*, petrosquamous sinus, and *squ. t.* temporal squama extending far downward.

Blood Supply.—The blood supply of the middle ear did not show any particular abnormalities. The internal carotid artery was of normal width and occupied its usual place. The trunk of the middle meningeal artery could not be found in the serial sections through the temporal bone, and the foramen spinosum was absent. In many of the sections arterial branches were seen on the outer surface of the dura; these seemed to represent branches of the middle meningeal artery, but

their place of origin could not be determined. The superficial petrosal branch in normal cases originates from the middle meningeal artery, enters the facial canal through the hiatus and anastomoses with the terminal twigs of the stylomastoid artery (fig. 7). In this case, however, it originated in the internal auditory artery and accompanied the facial nerve on its way from the internal auditory meatus to the middle ear (fig. 3).

The petrosquamous sinus was well developed (figs. 1 to 7) and left the cranial cavity through the posterior part of the foramen ovale.

Inner Ear.—The osseous capsule showed normal configuration. It contained an ovoid-shaped cartilage "rest" in its posteroinferior part. It lay in the outer parts of the enchondral layer (fig. 3) and extended from there to the periosteum at the anterosuperior circumference of the jugular foramen in a posteroinferomedial direction through the periosteal layer. At its base, it showed progressive ossification from the enchondral layer. That part which bulged into the periosteal layer was covered with a thin layer of connective tissue, and there was no connection between the cartilage and the surrounding bone.

The membranous labyrinth showed no abnormalities.

Right Temporal Bone (horizontal serial sections).—All parts showed normal configuration and structure. The middle ear cavity showed a very well developed lumen, on this side, too. The large cartilage rest described on the left side could not be seen.

Summary of Anatomic Findings.—Briefly summarized, there was in this case a normal right ear and the following malformation of the left ear: moderately severe malformation of the auricle; complete absence of the external auditory meatus and the drum membrane; absence of the tympanic bone with downward extension of the squama and upward extension from the floor; hypoplasia of the anterior part of the squama with backward extension of the greater wing of the sphenoid underneath the squama; a low origin of the tegmen from the lateral labyrinthine wall; hypoplasia of the osseous portion of the tube, opening into the lower portion of the well developed middle ear lumen, with the upper part of the latter forming an anterior recessus; upward and forward extension of the slightly hyperplastic upper end of the styloid process which is fused with a malformed outer ossicle replacing malleus and incus; connection of the malformed outer ossicle and of the capitulum of the stapes with the wall of the facial canal; hypoplasia, lateral displacement and abnormal insertion of the tensor tympani muscle; an anomalous muscle in the tegmen; anomalous course of the facial nerve through the middle ear; absence of the lesser superficial petrosal nerve; absence of the foramen spinosum and anomalous course of the middle meningeal artery; origin of the superficial petrosal arterial branch from the internal auditory artery; well developed petrosquamous sinus, leaving the cranial cavity through the foramen ovale; absence of the parotid gland, and a large cartilage "rest" in the enchondral part of the osseous labyrinthine capsule near the anterosuperior circumference of the jugular foramen.

The malformations of the ear were associated with bilateral cleft palate and multiple anomalies of the inner organs.

COMMENT

Most of the malformations just enumerated can be explained as the result of developmental disturbances of the derivatives of the posterior ends of the first and second branchial arches, of the adjacent structures and of the first branchial pouch and cleft.

Abnormal differentiation of the upper end of the branchial cartilage of the first arch was what led to the formation of the anomalous outer ossicle, which evidently represented the fused incus and malleus. It consisted mainly of the incus, which showed a well recognizable short and long process, and a body, with which the head of the malleus was fused. The manubrium, short process and anterior process of the malleus were absent. Lack of formation of the membranous bones in the neighborhood of the upper end of Meckel's cartilage undoubtedly caused the absence of the tympanic ring and the anterior process of the malleus. The place usually occupied by the tympanic ring was partly filled by a short downward extension of the squama and a short bony lamella extending upward from the lateral edge of the bony floor of the middle ear. The malformation of the upper end of the branchial cartilage of the second arch chiefly affected the upper end of the main part of this second arch, the so-called laterohyal and the upper end of the so-called stylohyal.

In normal circumstances the laterohyal forms the eminentia styloidea and participates in the formation of the lower part of the facial canal; from the stylohyal the styloid process is derived. The upper end of the laterohyal fuses with the labyrinthine capsule after the disappearance of its connection with the stapes (interhyal); the lower end fuses with the upper end of the stylohyal. It seems that in the case being discussed the upper end of the laterohyal did not fuse with the labyrinthine capsule; instead, it had grown forward and upward toward the incudomalleolar anlage and eventually fused with it. It did not participate in the formation of the facial canal and could not possibly have done so, even if it had remained in its normal location, because of the abnormal course of the facial nerve. The border between the laterohyal and stylohyal was most probably located at the place where the cartilage bar changed its course from backward and upward to upward and forward.

The disturbances in the development of the branchial skeleton also led to anomalies in the connection between the anlage of the incus and stapes, which, as a rule, is already present in early embryonic life (embryos of 17 to 18 mm.). Instead of an incudostapedial joint, a bony bridge from the lower end of the incus and from the capitulum of the stapes to the medial tympanic wall was formed.

The hypoplasia and the abnormal course and insertion of the tensor tympani muscle point to disturbances in the differentiation of the mesenchyme of the first branchial arch from which this muscle develops. The anomalous muscle in the tegmen indicates by its innervation through a branch of the trigeminal nerve that it was derived from the same source. I have observed similar muscles in other malformed temporal bones (Altmann, 1932).

The abnormal course of the facial nerve, the nerve of the second branchial arch, was evidently a consequence of the abnormal developmental changes within the latter.

The abnormal course of the middle meningeal artery, with the consequent absence of the foramen spinosum, can also be explained through anomalies within the second branchial arch. The middle meningeal artery is originally a branch of the stapedial artery, which takes its origin from the so-called later hyoid artery (Altmann, 1947).

It is impossible to state where the middle meningeal artery entered the middle fossa in the case described in this paper. In 2 cases with absence of the foramen spinosum (Toida, Low), it was assumed that the artery had originated from the sphenomaxillary portion of the internal maxillary artery, had entered the orbit through the inferior orbital fissure and from there the middle fossa, either through the superior fissure or the foramen meningo-orbitale in the greater wing of the sphenoid.

The origin of the superficial petrosal branch from the internal auditory artery instead of from the middle meningeal artery deserves special attention. Origin of the entire middle meningeal artery from the internal auditory artery has been described previously by me (Altmann, 1932), also in a malformed temporal bone. This has been explained as a persistence of a so-called presegmental artery accompanying the acusticofacial nerve, with formation of a connection between this vessel and the supraorbital branch of the stapedial artery (Altmann, 1947). Although the condition in this case cannot be completely clarified, it seems very probable that the superficial petrosal branch here represents a persistent presegmental acusticofacial artery. This persistence seems to have been combined with anomalies in the junction of the anastomotic branch between the external carotid artery and the stapedial artery. This anastomotic branch later became the internal maxillary artery.

A persistent petrosquamous sinus is relatively frequent, even without any other malformations (Zuckerkandl, Knott, Cheatle, Streit Vernieuwe, Laff and others). After leaving the lateral sinus, it usually crosses the ridge of the petrous bone, follows the course of the petrosquamous fissure and leaves the middle fossa either through the spurious jugular foramen or with the middle meningeal vein through the foramen spinosum or, in rare instances, through the mastoid foramen. Departure through the foramen ovale, as found in the case described in this paper, has not yet been reported so far as I am aware.

Absence of the lesser superficial petrosal nerve is not uncommonly observed in such malformations (Altmann, 1933).

It cannot be decided whether the parotis was actually completely absent or only hypoplastic, as reported in some cases by me (Altmann, 1933).

In the malformation of the auricle both the mesenchyme of the first and that of the second branchial arch, which normally form the auricle, participated. The latter was only slightly smaller than normal in the case presented here; the different parts could be recognized, and a real defect was not found. These conditions represent a so-called first degree of microtia (Marx).

The absence of the external auditory meatus was due to the lack of development of the primary auditory meatus and of the meatal plate. Owing to the absence of the latter, which forms the inner part of the meatus, a drum membrane was not formed.

The hypoplasia of the osseous eustachian tube was due to an impeded development of the tubotympanic pouch. When considering the condition of the middle ear, one must distinguish between the anlage as a whole and the epithelium-lined cavity, the actual derivative of the first branchial pouch. The middle ear anlage in this case was smaller than usual and especially showed a diminished width. This is easily demonstrated by the fact that structures which normally are found within the cavity, such as the chorda tympani, were here found outside of it. The height of the anlage was also diminished, as evidenced by the low origin and the downward slanting course of the tegmen.

Notwithstanding the hypoplasia of the whole anlage, the epithelial part showed the same excellent pneumatizing power as on the other side. The combination of the marked pneumatizing power with the primary hypoplasia may account for the formation of the anterior tympanic recessus and the atypical opening of the tube into the middle ear cavity.

A review of the reported observations reveals the interesting fact that in almost all the cases with hypoplasia of the middle ear, alone or together with hypoplasia of the tube, there was a mastoid process of normal size and, as a rule, with good development of the pneumatic cells. This is regarded as due to the effect of a localized damaging factor which acts on a circumscribed area only (Altmann, 1933).

The cartilage "rest" in the enchondral capsule was due to a retardation of the ossification in a localized area of the capsule. I have observed similar foci in other instances also (Altmann, 1932).

Associated with the malformations of the two branchial arches were disturbances in adjacent parts of the skull, hypoplasia of the squamosum with normal development of the zygomatic portion and excessive growth of the greater wing of the sphenoid.

An excessive backward extension of the greater wing of the sphenoid beyond the anterior border of the squama had been described previously by me in malformed temporal bones (Altmann, 1933). In these cases the squama was either hypoplastic, as in the observation described in this paper, or normal in size.

An explanation of this anomaly is difficult. Comparative anatomic studies have shown that the lateral part of the middle fossa of the mammals represents a region which in lower vertebrates is outside the cranial cavity. Because of the marked increase in size of the brain in mammals, the original lateral cranial wall has disappeared and the brain has been extended into an area which originally was situated outside the primordial cranial cavity. A secondary lateral wall of the cranial cavity is thus formed by the greater wing of the sphenoid bone (Matthes, Stadtmüller). The squamosum which in lower vertebrates is a membranous (dermal) bone of the otic capsule and of the palatoquadrate bar, retains in mammals also its relationship to the otic capsule, for it becomes intercalated between the parietal bone, petrous process of the temporal bone and the greater wing of the sphenoid. Its participation in the formation of the lateral wall of the skull shows great variations, however, in different species of mammals. It is, for example, almost completely excluded from the skull in Ruminantia and Cetacea but participates extensively in others (Stadtmüller).

It is possible that the anomaly in question reflects the fact that the participation of the squamous process in the formation of the lateral wall of the skull is not a primitive condition but a later acquisition of the mammalia which shows a great variability in the different species.

Complete absence of the external auditory meatus, as in the case just described, is the most frequent finding in congenital atresia. In others, the outermost part of the meatus is present.

In one group of cases, however, which represent the mild degree of malformation (Altmann, 1933), either the entire canal, although hypoplastic, or at least its inner part, is present. The tympanic bone is hypoplastic and somewhat misshapen and the drum membrane smaller than normal. The tympanic cavity is normal in size or hypoplastic. Its contents show malformations of varying degree.

Altogether 15 sufficiently well described cases (17 temporal bones) have been reported (summarized in the table).

The cases in which the external auditory meatus was completely absent, possibly with exception of the outermost part, I have divided into two groups, representing the medium and severe degree of malformation (Altmann, 1933).

The severe degree, which is of less interest in this connection, is represented by 10 cases in which the tympanic cavity was completely absent or extremely hypoplastic (the table).

The medium degree, to which the case described in this paper belongs, shows the greatest structural variations. The tympanic cavity is, as a rule, diminished in size and its contents deformed in varying degree. The lateral wall of the tympanic cavity forms the so-called atresia plate which is either completely or partly osseous. The tympanic

bone is present in some cases and missing in others. If it is present, it is badly misshapen, often platelike; frequently it contains at its center a membrane-like mass of connective tissue which is continuous with the connective tissue occupying the place of the missing external auditory meatus.

Regardless of whether a malformed tympanicum is present or not, the upper end of Reichert's cartilage might show anomalies. It might be abnormally situated and hyperplastic and might form the main part of the atresia plate. It is difficult to determine which particular part of Reichert's cartilage is malformed, particularly in older subjects, in whom extensive ossification has already taken place.

Cases of Congenital Atresia, Grouped According to the Severity of the Malformations and According to the Structure of the Atresia Plate

	Malformations of Medium Degree				
	Malformed Tympanic Bone Present		Tympanic Bone Absent		
Malformations of Mild Degree	Atresia Plate Formed by the Tympanic Bone	Atresia Plate Formed by the Tympanic Bone and the Upper End of Reichert's Cartilage	Upper End of Reichert's Cartilage Hyperplastic	Reichert's Cartilage Not Hyperplastic; Processes from the Squama and the Tympanic Floor	Malformations of Severe Degree
Heusinger (right and left) Hyrtl (case 1 to 3) Birnbaum Meyer Landauer Kaufmann (case 2, left) Krampitz (right) Alexander and Benesi (case 2) Arione (right) Altmann, 1933 (case 1, right and left; case 2, left) Nager (left) Druss and Allen	Ranke (case 2) Broca and Lenoir Hoepfner Takanarita Arione (left) Marx, 1926 Lüscher (case 2) Fraser and Davis (left) Přecechtel Brühl (right and left) Nager (right)	Lüscher (case 1)	Alexander and Benesi (case 1) Marx (cases 1, 2) Altmann, 1933 (cases 3, 4, right and left; 5, 6, right and left) Kelemen Altmann (present case)	Sailly Hagens, 1932, 1933 Altmann, 1933 (cases 7, 8 right and left) Cantele Ricci	Lucae Virchow, 1864 Wreden Moos and Steinbrügge Ranke (case 1) Kaufmann (case 2, right) Marfan and Delille Leblanc Hofmann Altmann, 1933 case 2, right)

A review of the suitable cases shows that in some of them, such as in the observation reported in this paper, the laterohyal had grown upward and forward toward the tegmen and the outer two ossicles. In others, the hyperplasia and the anomalous growth were found to have affected the upper end of the styloid process, as pointed out by Marx. In rare instances the laterohyal was malformed but in its normal place (Altmann, 1933, case 6, both sides). In order to avoid misunderstandings, it must be stressed that the term laterohyal is here used according to Broman, who designated by this term the part of the branchial arch skeleton which lies laterad to the facial nerve and which, in normal circumstances, connects the labyrinthine capsule with the main part of the branchial skeleton, with the stylohyal. It seems logical to agree with Marx that it is not permissible to call all the derivatives of Reichert's

cartilage with the exception of the stapes, laterohyal, as Alexander and Bénesi and other authors have done. In some of the observations, such as those described in this paper, the descending part of the facial nerve takes an anomalous course and leaves the middle ear at a point more forward and upward than usual; in others, its course is more or less normal. Since the laterohyal normally plays an important role in the formation of the lower part of the facial canal, the change in the course of the facial nerve might point to anomalies of the laterohyal, particularly in those instances in which the lower part of the nerve shows an anomalous course. In these cases the laterohyal may possibly participate in the formation of the atresia plate; in the cases with a normal course of the nerve, it seems more probable that the styloid alone is malformed.

The chorda tympani, in the course of normal development, always lies laterad to Reichert's cartilage. It has been shown by Marx that in cases in which the atresia plate is formed by the hyperplastic upper end of Reichert's cartilage alone the chorda is to be found running along the outer surface of the plate. This was also true in the case reported in this paper. It is self evident that the plate in these cases does not occupy the site of the tympanic membrane but lies mediad to it and that the tympanic cavity represents only the medial part of the tympanic cavity of normal ears.

If the tympanic bone is defective, outgrowths are formed from the squama and from the floor of the tympanic cavity, which extend downward and upward respectively and diminish or close the defect of the lateral wall. The development of these two processes seems to be in inverse proportion to the degree of enlargement of the uppermost part of the skeleton of the second branchial arch. It takes place gradually during fetal and postfetal life and most probably represents a proliferation *ex vacuo* into the space normally occupied by the tympanic bone. From the course of the chorda tympani in cases without hyperplasia of Reichert's cartilage, it may be concluded that there the atresia plate usually lies more medial than the normal drum, but not so far medial as the hypertrophied upper end of Reichert's cartilage (Altmann, 1933).

Altogether 28 cases (32 temporal bones) belonging to the second degree of malformation permit a detailed genetic analysis of the atresia plate (the table). In 12 of them a malformed tympanic bone was present. In 11 the atresia plate was formed by the tympanic bone alone or together with a mass of condensed connective tissue. In 1 case the plate was formed by the tympanicum together with the hyperplastic upper end of Reichert's cartilage. In 16 cases, the tympanic bone was completely absent. In 9 of them, the upper end of Reichert's cartilage was hyperplastic (laterohyal or stylohyal); in addition, there might be formation of processes from the squama downward and the floor of the

tympanum upward. In 7 cases there was no hyperplasia of the derivatives of the second branchial arch but only formation of processes from the squama and the floor of the tympanum.

Malformations of the ossicles, particularly of the malleus and incus, are commonly observed in such cases. Of special interest with regard to the possibility of improvement of hearing through surgical procedures is the presence of bony bridges between the medial wall of the promontory and the malformed outer ossicle and the head of the stapes. Both types of bridges were also present either singly or combined in several other cases reported in the literature.

Malformations of the inner ear were absent in the case described in this paper. They were, however, found in one third of the cases and showed a great variability in their location and degree.

Although in the case in question the left ear was malformed, the right side is, as a rule, much more frequently affected. This is shown even in prehistoric skulls afflicted with this malformation (Hrdlička). No satisfactory explanation has yet been given for the predominance of the right side.

There is no definitely proved sexual incidence in these malformations.

The evidence of heredity is somewhat scanty, at least in man (Sedgwick, Windle, Krampitz, Torrigiani, Frenzel, Eckert-Möbius, Schwarz). In animals, among which cases have been reported in pigs, goats, sheep, cattle, horses, hares, rabbits and mice, there is definite evidence of hereditary transmission in many instances; in mice the inheritance of congenital atresia follows a recessive trait (Feldman).

Very often, as in the case described in this paper, the malformations are not confined to the ear but affect adjacent parts of the skull, other parts of the branchial arches, the second branchial pouch or other structures of the head. The following malformations should be mentioned: hypoplasia of the mandible, alone or combined with other malformations of the face (dysostosis mandibulofacialis—Franceschetti and Zwahlen), defective development of the ramus mandibulae and the temporomandibular joint; hypoplasia or defect of the zygomatic arch, hypoplasia of the hard palate, hypoplasia or defect of the velum palatinum; absence of the anterior tonsillar pillar and of the tonsil; teratoid tumors originating from the tonsil, heterotopic thymus tissue in the middle ear, fissures of the face, particularly transverse fissure, cleft lips and palate, hypoplasia of one half of the face (facial hemiatrophy) sometimes combined with congenital facial paralysis, choanal atresia, hypoplasia of the parotid gland, coloboma of the eyelid or congenital narrowing of the lid cleft.

In addition, accompanying malformations in other, more remote, internal organs and in various parts of the skeleton are often found. Among the skeletal malformations two will be mentioned because of

their relative frequency: dysostosis craniofacialis (*maladie de Crouzon*) (Nager) and defects of the radius and the distal skeletal parts connected with it (Essen-Möller).

Because genetically different formations, which are nevertheless situated in the same area, are found to be malformed in cases of congenital atresia, one may believe that the malformations were caused by a damaging factor of unknown nature which was present in a circumscribed area during early development. Such a group of coordinated malformations confined to the same region comprise what Virchow called a *Störungskreis*.

The circumscribed area in which the effect of the supposed damaging factor becomes manifest is well demonstrated by the cases in which the tympanic cavity and the neighboring systems of pneumatic cells are poorly developed, but the eustachian tube, the antrum and the mastoid cells are normal. In such cases it can be assumed that the damaging factor has acted only in that portion of the tubotympanic tube which later becomes the middle ear.

The question of the cause of the congenital atresia of the ear remains undecided in spite of that increased knowledge of the physiology of early embryonic development which has greatly helped in the interpetation of many varieties of congenital malformations in this field. Our knowledge is based mainly on evidence gained from the results of experimental studies in lower vertebrates, particularly in amphibians. It was demonstrated by Spemann and his school that the normal development of the entire body takes place under the inductive influence of the so-called organizers. These are, generally speaking, areas of the embryo which exercise a specific regulatory influence on morphogenesis by producing certain chemical substances (evocators) which bring about the differentiation of the various organs and tissues. The primary organizer material is derived from the dorsal lip of the gastrula. It gives rise to a head organizer, which induces the differentiation of head, brain and sense organs, and to a trunk organizer, which induces the differentiation of the trunk. In the course of this embryogenesis, organizers of lower grade (secondary, tertiary, etc.) are formed. These exert a more limited and specific inductive influence on organ and tissue differentiation in successive developmental stages. The ear vesicles develop under the inductive influence of a second grade organizer of the hindbrain and the head mesoderm; the primary inductor seems to be the head mesoderm (Harrison, Pasteels and others). The otic capsule is induced by a third grade organizer, the otocyst and its derivatives. Keller, after a review of the literature and a genetic analysis of typical malformations of the head in rabbits, came to the conclusion that the development of the head in mammals is governed by the same principles as in amphibians. According to him, the development depends on the

presence of normal organizers; if the latter are damaged, faulty development of the affected areas will be the result.

Among the various factors which could exert a damaging influence on mammalian organizers, the genetic factors should first be mentioned.

Gene mutations occur not infrequently in mammals, including man. If they lead to malformations which are incompatible with life, they are called lethal; if they lead to early death, they are called sublethal mutations (Wriedt, Eaton, Mohr, Lerner, and others). The abnormal genes show a specific action on certain areas and at certain stages of embryonic development (primary organizer, second grade organizers, etc.) (Toendury).

The combination of atresia of the ear with other malformations in the head region can be regarded as organizer damage with subsequent manifestation in various parts of the head. Combinations of atresia with malformations of other parts of the body could be accidental; if they occur frequently, such as combination of congenital atresia with defects of the radius, the possibility of gene linkage should be considered, particularly if the malformations are of a hereditary nature. In other instances, a single gene has been shown to produce a wide variety of effects, some of which may be shown to be caused by others but the totality of which is difficult to relate to any common factor. In these cases with "pleiotropic" gene action, it is likely that the fundamental anomaly is metabolic, manifesting itself in different ways (Needham). Not all the syndromes of multiple congenital defects, however, are genetically determined. Environmental interference with the early development of the embryo may also result in multiple congenital malformations. Repeated appearance of congenital malformations in a pedigree may be due not only to inheritance of abnormal genes but also to repeated exposure of developing embryos to the same adverse environmental factors.

The normal mode of action of the genes depends on the presence of normal relation between nucleus and cytoplasm and of normal environment. Anomalies, not only of the genes but also of one of the other factors, may result in faulty differentiation. In certain instances the same type of malformation can even be produced by anomalies of either the genes or the other factors; here the malformations are called phenocopies.

Among the environmental factors which may produce malformations in mammals, the chemical factors are of particular interest. The action of trypan blue deserves special attention because it frequently produces congenital atresia of the ear.

Gillman and his collaborators found that the subcutaneous injection of 1 cc. of an aqueous solution of trypan blue every two weeks into female rats before conception and pregnancy led to a high incidence of such

congenital malformations as hydrocephalus, spina bifida, eye defects, and a lesser incidence of tail defects, meningocele, harelip, cleft palate, cranioschisis, ear defects, imperforate anus, club feet and dislocations of the forelimbs and hindlimbs. If the animals received the injections on the seventh or sixth day before conception as well as on the seventh or eighth day of pregnancy, the incidence of malformations was 80 per cent in the former instance and 65 per cent in the latter.

Malformations of the ear were found in 5.9 per cent of the total number of abnormal animals. The pinna was lacking altogether or was represented by a small tubercle. No external auditory meatus could be detected. In 1 case an additional tubercle was present on the pinna of the ear. The malformed ears were either solitary or combined with other malformations, such as hydrocephalus, defects of the eyes or both or with defects of the skull.

Trypan blue is absorbed by the albumin fraction of the plasma protein and produces a metabolic disorder in the animals given the injections. The dye does not enter the fetus; so the malformations were evidently a result of metabolic disease in the mother. The fact that the highest incidence of malformations occurred when the mothers were given injections on the seventh or eighth day of pregnancy does not necessarily mean that certain tissues of the embryo are more vulnerable at certain developmental periods than at others. The supposed metabolic disorder could lead to disturbances in the implantation of the embryo into the uterine wall, which takes place at that particular time, and which is a complicated process necessitating various types of adjustments in the embryonic membranes and in the maternal tissues. It is much easier to relate the critical period of vulnerability of the rat embryo to the time of implantation than to the degree of growth and differentiation of those primordia which later undergo a perverted development. Changes in the metabolism of the chorionic villi at this early stage, for example, may profoundly modify the subsequent growth of the embryo and lead to malformations.

In other instances chemicals may exert an injurious influence on second or third degree organizers or their evocators which regulate the embryonic development in the later stages.

Infectious factors may also affect the embryo. One disease, maternal rubella, is of particular interest for the otologist.

Gregg was the first to notice that infection with German measles in the first months of pregnancy led to anomalies in the offspring in a great number of instances. The defects were located mainly in the central nervous system, the sense organs (eye, ear), and the heart; less frequently in other organs, e. g. the teeth.

The histologic examination of one ear by Carruthers, although an incomplete one, showed that the changes were confined to the membranous parts of the inner ear.

Nothing definite is known yet of the mode of action of the rubella virus.

Nutritional factors also seem to play an important role, although so far only malformations of the auricle have been produced in this way in a few instances.

Vitamin A deficiency in the diet of pregnant animals leads to various malformations in the offspring. Hale produced anophthalmia, microphthalmia, accessory auricles, cleft palate and lip, subcutaneous cysts and displaced kidneys in pigs. Warkany and Schraffenberger observed malformations of the eye with associated thoracic and abdominal abnormalities in rats.

Riboflavin deficiency leads to multiple skeletal deficiencies in rats, including cleft palates (Warkany and collaborators).

Irradiation of pregnant mice and rats with roentgen rays and radium results in various malformations in the offspring, such as defects of the eyes, the brain (pseudencephaly) and the skeleton, including cleft palate, etc. (Bagg, Bagg and Little, Bailey and Bagg and others). These malformations are regarded as due to the direct effect of the rays on the tissues of the embryo. Gillman and his collaborators recently reconsidered the possibility of an indirect effect from the radiation, leading primarily to metabolic disturbances of the mother.

Irradiation of male animals may result in hereditary changes in the offspring, but these are regarded as the result of reciprocal gene translocation rather than of gene mutation (Snell and collaborators, P. Hertwig). Marked anomalies of the brain may be found; in other instances anomalies of the ears were produced (spinning and shaking mice with syndactylism, P. Hertwig).

The importance of mechanical factors, such as amniotic bands or adverse mechanical conditions during ectopic pregnancy, seems to have been overestimated in the past. Since the discovery of other causative factors, less emphasis has been placed on mechanical ones.

A summary of the foregoing material shows that congenital atresia of the ear need not necessarily and invariably be the result of genetic changes; there are good reasons for assuming that in certain instances metabolic disturbances during early pregnancy may produce the same type of malformations, sometimes even in combination with other, seemingly unrelated, anomalies.

Even in a case such as the following one recently observed in Babies Hospital, no definite decision about the etiology can be made.

A woman gave birth to a girl with multiple malformations, among them bilateral cleft lip and palate and atresia of the anus with rectovaginal fistula. One year later, she again gave birth to a girl with multiple malformations; among them there was again bilateral cleft palate, atresia of the anus with rectovaginal fistula and, in adition, multiple malformations of the eyes and bilateral atresia of the external auditory meatus.

A carefully compiled family history revealed the following facts: The father was 31 years of age, the mother was 35 years of age and both were in good health. The father was in the South Pacific during the war and had "dengue and yellow jaundice" there. There was, however, no recurrence of either. There was no history of venereal diseases, exposure of either parent to roentgen rays, radium or atomic energy. Both pregnancies ended at full term; there were no diseases during pregnancies, no abortions and no miscarriages. There was no evidence of malformations in the father's family for five generations or in the mother's family for four generations. The paternal grandfather had a mild diabetes of twelve years' duration. No family history of allergies or of gastrointestinal or genitourinary diseases was obtained.

The assumption that the malformations in this case are caused by a recessive sublethal gene is very tempting, but, as has already been stated, repeated exposure of developing embryos to the same adverse environmental factors may have the same effect.

The hearing in cases of congenital atresia, aside from the severity of the malformations of the external and middle ear, depends on the condition of the inner ear. If the latter is intact, the hearing is, as a rule, not too severely impaired; hence, even in cases of bilateral involvement, ordinary conversation can be understood well enough. As a result, the development of speech in the child will be unhampered. If, however, the labyrinth is also affected, the hearing loss will be more profound.

Attempts to improve the hearing in congenital deformities by operative intervention should be confined to cases in which one can be reasonably sure that the inner ear is intact. But even in these cases the optimism of many authors regarding the chances for success seems hardly justified. Because of the great variety of changes in the middle ear, it is practically impossible to recognize those cases which are apt to respond to surgery with a reasonable degree of certainty. Those who are thoroughly familiar with the anatomic changes in these cases will be able to determine in a certain number of instances, by a combined clinical and roentgenologic examination, the approximate type of malformation (Politzer and Mayer, Mittermaier, Leroux and Cottenot, Camp and Allen and others) but not the exact condition. Minute deformities will, as a rule, escape detection; they are, however, sometimes of decisive importance in determining the extent of improvement in hearing to be gained by surgery. Fixation of the stapes, that is, by bony bridges to the medial wall or bridges between the outer ossicles and the medial, superior or outer wall, would remain undiagnosed by present methdos of clinical examination.

In cases with unilateral malformation the necessity of improving the hearing will rarely arise and an operation will be unnecessary unless a surgical mastoiditis has developed or a congenital cholesteatoma is present or suspected. In cases with bilateral malformation and seem-

ingly intact inner ears, a bone conduction aid might, in view of the uncertainty of the success of an operation, be preferable in many instances. If, however, an operation is decided on, the technic must be varied in detail, according to the special conditions met in each individual case.

The principle of these operations consists in opening of the mastoid through a retroauricular or an endaural incision (Pattee) or through a combined retroaural and endaural incision (Ombredanne). Then the mastoid cells, if present, are removed, the antrum located and opened, the lateral semicircular canal identified and the outer ossicles visualized. Removal of at least the incus seems essential for the success of the operation, because with the drum membrane almost invariably absent and the ossicles practically never free of at least minor malformations, the ossicular chain, even if present in all its parts, serves no useful purpose and may, indeed, impede the transmission of air-borne sounds to the inner ear. This is particularly the case when bony bridges are present between the malleus or incus and the walls of the middle ear. The main danger in the postoperative course is the tendency of the newly created opening into the mastoid to narrow and close. Retention of secretions in the operative cavity with all its consequences will be the result. In order to prevent this most undesirable development, a plastic flap is formed; however, because of the absence of the skin of the external meatus, the flap will be small and in many instances insufficient to prevent eventual closure of the opening. It is, therefore, advisable to cover the operative cavity with Thiersch grafts which are kept in place, according to most authors, with packings. Pattee opens the antrum just far enough to remove the incus. Thiersch grafts are then placed in the cavity and over the opening into the middle ear. The edges of the graft are then sutured to the edges of the skin incision. The grafts are kept in place by wet cotton packing, which is removed after five to seven days. If the opening into the middle ear is not too large, the middle ear mucosa grows quickly over the unlined under surface of the graft, according to this author; otherwise it would slough. Ombredanne has suggested the use of a Stent mold to keep the cavity open. In a case in which I operated, a paraffin mold of the cavity was first made and then the cavity was refilled with melted paraffin. The paraffin mold was then reproduced in acrylic resin; the paraffin was removed from the cavity and the surface of the acrylic mold covered with Thiersch grafts and put back into the cavity. The acrylic mold was worn by the patient until the cavity was completely epithelized.

But, even if all the necessary precautions are taken and the technical result is perfect, the hearing still remains unimproved in a considerable number of cases, including those in which fixation of the stapes or other abnormalities in the windows and their niches are present. I cannot,

therefore, agree with Pattee's claim that after an operation "theoretically, therefore, the hearing should be improved to about the level expected from the fenestration operation."

Ombredanne (1947) recently advocated in cases of congenital atresia a fenstration of the lateral semicircular canal and covering of the fistula with a retroauricular skin flap. He reported good results in two operations performed in children.

Fenestration is undoubtedly of value in cases with fixation of the stapes but unnecessary in all the others. Because of the practical impossibility of differentiating clinically between the two groups, it seems preferable to do the usual operation first. If, after complete epithelization the hearing is not improved, a fenestration could be performed as a second stage operation. In this instance, the prospects of permanent patency of the fenestra would undoubtedly be much greater than in Ombredanne's one stage operation with a thick flap from the retroauricular skin.

The question of when and how a plastic reconstruction of the malformed auricle should be undertaken belongs, in all its technical and psychologic aspects, to the domain of the plastic surgeon and not of the otologist. It will, therefore, not be discussed here.

SUMMARY AND CONCLUSION

A histologic examination of a congenital atresia of the left ear in a newborn girl with multiple malformations showed complete absence of the external auditory meatus, the drum membrane and the tympanic bone, malformation of the outer ossicles and an osseous bridge between the capitulum of the stapes and the facial canal. The resulting defect in the lateral wall of the tympanum was partially filled by an upward and forward extension of the upper end of the styloid, a downward extension of the squama and an upward extension from the floor of the middle ear. In addition, many other anomalies were present.

Most of these malformations can be explained as the result of developmental disturbances of the derivatives of the posterior ends of the first and second branchial arches, of the adjacent structures and of the first branchial pouch and cleft.

Fifty-three sufficiently well described cases of congenital atresia have been reported so far. According to the severity of the malformations, they can be divided into three groups; those of a mild degree (15 cases), medium degree (28 cases) or severe degree (10 cases).

In the cases of medium degree, to which the case described in this paper belongs, the lateral wall of the tympanum, the so-called atresia plate, shows great structural variations. The tympanic bone, although malformed, participated in its formation in 12 cases and was absent in 16 cases. In 9 of the latter cases the upper end of Reichert's cartilage

was hyperplastic; in 7 there was only formation of processes from the squama and the floor of the tympanum.

Hypertrophy of the upper end of Reichert's cartilage is a relatively frequent feature but not an essential characteristic of these malformations, as is assumed by some authors.

The cause of the malformations remains undecided. A review of the more recent work on experimental mammalian teratology shows that not only genetic but also environmental factors acting on the developing embryo must be considered as possible causes.

The chances for an improvement of hearing by operative intervention are doubtful, even in cases with an intact inner ear. This is due to the frequency of bony bridges between the stapes and the medial tympanic wall and to other minute deformities which might escape detection.

If an operation is decided on, a radical mastoidectomy with endaural approach and removal of the outer ossicles seems the method of choice. Skin grafts should be put into the cavity and kept in place by a mold. This will help to prevent postoperative stricture of the newly created opening. If the hearing is not improved after the operation, the possibility of fixation of the stapes should be considered. This could be circumvented by fenestration of the ampullated end of the lateral semicircular canal in a second stage operation.

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GLOSSOPHARYNGEAL NEURALGIA

Tic Douloureux of the Ninth Cranial Nerve

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TODAY, glossopharyngeal neuralgia is recognized as a major type of paroxysmal pain involving the distribution of the ninth cranial nerve. This has not always been so. For many years it was mistaken for trigeminal neuralgia, although the pain was not relieved by a partial or complete division of the posterior root of the gasserian ganglion.

The course of the glossopharyngeal nerve was described by Galen [1] and the nerve separated as a distinct entity by Fallopius, but the actual functions were unknown until recent years. In 1910, Weisenburg [2] described the symptoms of glossopharyngeal neuralgia due, in his case, to a tumor in the cerebellopontile angle pressing on the ninth nerve as shown at autopsy. Sicard and Robineau [3] in 1920 described true glossopharyngeal neuralgia but were not certain of its purely ninth nerve origin. Doyle [4] and Adson,[5] of the Mayo Clinic, were the first to report cases [4] and to operate [5] in such cases in this country. Adson first tried the extracranial approach, but from his studies in the cadaver he advocated the intracranial approach for permanent cure. Love [6]

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Read at the meeting of the Virginia Society of Ophthalmology and Otolaryngology, Winchester, Va., May 8, 1948.

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credited Adson (1925) and Peet [1] gave Dandy [7] (1927) credit for the first successful intracranial section of the ninth nerve for true glossopharyngeal neuralgia. The excellent monographs by Doyle, Adson, Dandy and Peet are comprehensive.

Glossopharyngeal neuralgia (although far less common than fifth nerve tic) differs from trigeminal neuralgia in only one important point, the distribution of the pain. In some instances neuralgia of both the ninth and the fifth cranial nerve may exist simultaneously. Peet, in a series of 14 patients, noted that 5 of them had trigeminal as well as glossopharyngeal neuralgia.

SYMPTOMATOLOGY

In general, the symptomatology of glossopharyngeal neuralgia is uniform. This is not difficult to understand, inasmuch as the sensory distribution of the glossopharyngeal nerve has been shown [8] to be the posterior third of the tongue, the lateral and posterior walls of the pharynx from the lower nasopharynx to the epiglottis, the tonsil, the anterior and posterior pillars, the orifice of the eustachian tube, the tympanic membrane (Jacobson's nerve) and a portion of the soft palate and uvula. Taste fibers supply the posterior third of the tongue. The trigger point is always in the distribution of the ninth nerve.

Severe paroxysmal pain is the outstanding feature of glossopharyngeal (tic) neuralgia. Talking, swallowing (especially cold liquids and ice cream), yawning, coughing, laughing or sneezing may precipitate the characteristic attack of sharp knifelike agonizing pain which usually lasts only a few seconds. In some instances the flashes of pain occur in succession for as long as two minutes. Intermission may vary from a few minutes to several hours or days. Remissions of weeks and months are common. A period of complete freedom from pain may exist for two or three years or longer.

DIAGNOSIS

The diagnosis of true glossopharyngeal neuralgia usually offers little difficulty. First, the complete history is obtained. In all the patients observed by us, attacks of pain occurred while the history was being obtained, thus presenting an opportunity for "on the scene" observation of the person's distress and behavior. Of the patients reported on here, all had unilateral distribution of the pain and, with but 1 exception, were very specific about the pain trigger zone.

7. Dandy, W. E.: Glossopharyngeal Neuralgia (Tic Douloureux), Arch. Surg. **15**:198-214 (Aug.) 1927.

8. Doyle.[4] Adson.[5] Love.[6] Dandy.[7]

Once the history is obtained, a thorough physical examination is made. At the time of the initial examination, use of nasal or pharyngeal anesthetic solutions is avoided if possible. When no obvious local etiologic factor related to the ear, nose, throat or neck can be found, the patient is asked to keep a written record of attacks of pain for twenty-four hours, noting duration and degree of pain, variations of distribution, if any, and interval of time between attacks of pain. Thereafter, cotton pledgets soaked in a 10 per cent solution of cocaine or 2 per cent solution of tetracaine hydrochloride U. S. P. (pontocaine hydrochloride®) and squeezed almost dry are applied directly to the region of the painful trigger zone as indicated by the patient. This procedure generally alters the pain within two or three minutes. Again the patient is requested to keep a written record of the attacks of pain for twenty-four hours. This permits a definite comparison and evaluation of the effect of anesthesia on the attacks of pain. Once the trigger zone is anesthetized, the paroxysms of pain are reduced in severity and in number for two to twelve hours or longer. Whenever any doubt exists about the diagnosis, this procedure may be repeated as often as necessary until a definite conclusion is reached.

DIFFERENTIAL DIAGNOSIS

In certain instances considerable study may be required for an exact diagnosis. In 1 of our patients the impression of the referring physician and the roentgenologist was that of a tumor of the upper portion of the esophagus because of apparent obstruction on swallowing (dysphagia). Barium sulfate could not be swallowed, leading the roentgenologist to believe that there was an obstructive lesion in the upper end of the esophagus. It was not until after esophagoscopy revealed the absence of an obstructing lesion that section of the left glossopharyngeal nerve was done. The patient could not swallow, not because of obstruction but because of severe pain in the throat.

There are several other lesions resembling tic which must be differentiated from glossopharyngeal nerve tic: 1. Tic douloureux of the third division of the fifth nerve. 2. Superior laryngeal nerve tic (vagus), as reported by Love [8] and co-workers,[9] causing external (lateral) throat pain. 3. Tic douloureux of the nerve of Wrisberg (nervus intermedius), or geniculate ganglion neuralgia, successfully operated on by Taylor [10] in 1910 and by Furlow [11] in 1941. Furlow

9. Smith, L. A.; Moersch, H. J., and Love, J. G.: Superior Laryngeal Neuralgia, Proc. Staff Meet., Mayo Clin. **16**:164-167 (March 12) 1941.

10. Cited by Hunt, J. R.: Geniculate Neuralgia (Neuralgia of the Nervus Facialis), Arch. Neurol. & Psychiat. **37**:253-285 (Feb.) 1937.

11. Furlow, L. T.: Tic Douloureux of the Nervus Intermedius, J. A. M. A. **119**:255-259 (May 16) 1942.

was the first deliberately to divide the nervus intermedius only for tic of that nerve due to pain confined to the ear (sensory root of the seventh nerve). If the trigger point of the pain is in the tragus of the external ear, this type of tic is the most likely diagnosis. 4. Neuralgia of the sphenopalatine ganglion (Sluder's). 5. Laryngeal crisis of tabes dorsalis. 6. The syndrome of lateral granular pharyngitis. There are two types of ninth nerve tic: (*a*) that confined to the ear alone (rare without pain in the throat [Jacobson's nerve neuralgia]), due to the involvement of the tympanic membrane (not the external ear) by Jacobson's nerve (a branch of the ninth) rather than involvement of the entire ninth nerve; (*b*) the common type, in which the pain in the throat predominates and appears first and in which the pain deep in the ear develops secondarily or radiates from the throat. Both of these types of ninth nerve tic are completely relieved by section of the ninth nerve alone, but when there is pain in the ear as well as in the throat it is probably better always to divide also the anterior two filaments of the tenth nerve (vagus) in every operation for ninth nerve tic.

If one is in doubt, because of predominant pain in the external ear or tympanic membrane, as to whether the pain is due to involvement of the ninth nerve (Jacobson's nerve) or to tic of the nerve of Wrisberg, operation under local anesthesia is advisable, so that the pain can be demonstrated by touching each nerve in turn with a forceps and dividing the appropriate one. Third division trigeminal nerve pain can be identified or eliminated by injection of alcohol, although it must be remembered that glossopharyngeal and third division (trigeminal) tic pain may occur simultaneously on the same side, as reported by Peet and Echols.[12]

TREATMENT

There is no satisfactory medical treatment for glossopharyngeal neuralgia. Hoover and Poppen [13] found inhalation of trichloroethylene helpful for relieving the pain for two or three hours in 2 patients. The application of local anesthetic agents, caustics and cautery treatments to the trigger zone may alter the attacks of pain temporarily but cannot be said to be curative. Intracranial section of the glossopharyngeal nerve offers the most satisfactory procedure for complete and permanent relief of the pain and is the only positive method of preventing recurrence.

12. Bancroft, F. W., and Pilcher, C.: Surgical Treatment of the Nervous System, Philadelphia, J. B. Lippincott Company, 1946, p. 283.

13. Hoover, W. B., and Poppen, J. L.: Glossopharyngeal Neuralgia, J. A. M. A. **107**:1015-1017 (Sept. 26) 1936.

In selected cases the operation can be performed with local infiltration anesthesia, but intratracheal administration of ether with tribromoethanol solution U. S. P. (avertin®) is preferred. The operative approach is identical to that used for division of the eighth nerve in Ménière's disease, i. e., a hemicerebellar exposure on the side of the patient's pain.

The dura is incised and the cisterna magna evacuated, followed by emptying of the cisterna lateralis. The auditory (eighth) nerve is usually identified first, but this is not essential. The ninth, tenth and eleventh nerves lie close toegther, about 1 cm. caudad to the eighth. The ninth is usually identified easily but occasionally with difficulty, as it may be rather closely approximated to the branches of the vagus nerve; furthermore, the ninth may be bifid. When identified, the ninth nerve is lifted on a nerve hook and divided with scissors, scalpel or the electrosurgical current. The anterior two rootlets of the vagus are also severed if the patient has a history of flashing pain in the eustachian tube and ear as well as in the throat. Following section of the ninth nerve, which is ordinarily the simplest of all posterior fossa operations performed by the neurosurgeon, there may be a slight transient dysphagia or dysarthria for three or four days if vagal rootlets have been divided.

Because the nerve has been sectioned central to its sensory ganglion (petrous), there can be no regeneration, just as in tic douloureux of the fifth nerve, in which operation the sensory root is divided between the gasserian ganglion and the pons. The mucous membrane supplied by the ninth nerve remains permanently anesthetic, and the gag reflex on that side is lost. Subjectively, the patient is rarely, if ever, aware of this postoperatively. This is in contrast to the typical consciousness of facial anesthesia following operation for fifth (trigeminal) nerve tic. No motor weakness can be demonstrated. There are no residual subjective symptoms of any kind, with the result that, practically speaking, there is no penalty to the operation, as there so often is following other operations on the cranial nerve. The loss of taste sense on the posterior third of one side of the tongue is not noticed by the patient. Results are usually very satisfactory.

Dandy [14] stated that in 2 of his early cases of glossopharyngeal tic the pain was diminished but not completely eliminated by cutting the ninth nerve only. The wound was reopened and the anterior filaments of the tenth nerve divided (one eighth to one sixth of the fibers of the tenth nerve), after which the pain was permanently abolished. At times both fibers (if the nerve is bifid) of the ninth nerve are incorporated with the tenth. Dandy in his last cases always divided the upper part (one sixth to one eighth) of the tenth nerve; no symptoms followed its inclusion in the section.

14. Dandy, W. E.: Surgery of the Brain, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, 1945, vol. 12, p. 188.

SUMMARY AND CONCLUSION

Glossopharyngeal neuralgia, or tic douloureux involving the glossopharyngeal nerve, has become a well established entity in the last twenty-five years. As a clinical syndrome it rightfully falls in the field of otolaryngology. However, since successful or specific operative treatment is the task of the neurosurgeon, most of the literature regarding this subject has appeared in medical literature other than that dealing with otolaryngology.

*Summary of Data on Eight Patients with Glossopharyngeal (Tic) Neuralgia Treated Surgically at the Medical College of Virginia from 1943 to 1948**

Sex	Age, Yr.	Side	Duration of Symptoms, Yr.	Distribution of Pain	Trigger Zone	Nerve Sectioned
M	30	L	5	Throat; ear	Tonsil fossa; lateral part of pharynx	Glossopharyngeal; vagus fibers
M	77	R	3	Base of tongue; lower jaw; ear	Tonsil fossa; rim of palate	Glossopharyngeal
F	62	L	4	Hypopharynx	Hypopharynx	Glossopharyngeal
M	39	R	3	Lower lateral part of pharynx; ear	Tonsil fossa; hypopharynx	Glossopharyngeal; vagus fibers
F	57	L	1	Posterior part of pharynx; rim of palate; ear	Tonsil fossa; palate; hypopharynx	Glossopharyngeal; vagus fibers
M	53	L	6	Lateral part of pharynx; ear	Lateral pharyngeal band	Glossopharyngeal
M	59	L	3	Ears; submaxillary triangles	Hypopharynx	Glossopharyngeal
M	50	R	⅙	Tonsil fossa; lateral part of pharynx	Tonsil fossa; lateral part of pharynx	Glossopharyngeal

* All patients were completely relieved, and no recurrence of symptoms was noted.

This report deals briefly with the cases of 8 Caucasian patients with glossopharyngeal neuralgia who were examined and treated by us within a period of five years. All recovered and were completely relieved by intracranial section of the ninth nerve and have had no recurrence of symptoms. There were 6 men and 2 women, the youngest 30 and the oldest 77 years of age. All had unilateral distribution of the pain, 5 having it on the left and 3 on the right.

In 3 patients with associated ear pain a few of the vagal fibers were also cut.

Glossopharyngeal (tic) neuralgia is a disabling disease which can be treated successfully by intracranial section of the glossopharyngeal nerve with no residual subjective symptoms.

INTRANASAL SURGERY OF THE MAXILLARY SINUS

HENRY M. GOODYEAR, M.D.
CINCINNATI

THE MAXILLARY sinuses are the most important of all the nasal sinuses. They are frequently infected, even in children, and with every infection of these sinuses there is always some extension of the infection to the ethmoid cells and often to the frontal sinus.

Thirty years ago it was commonly taught that the antrum was frequently infected by a downward flow of secretion from infected ethmoid cells or the frontal sinus, the antrum serving as a large cistern, catching the secretions from the sinuses above. It is now known that the reverse extension of infection is more apt to occur. If iodized oil is placed in the antrum and the patient's head is then lowered for even the matter of minutes, roentgenograms will show that the oil has migrated to the frontal sinus and ethmoid region.[1] This clearly indicates what may happen when a patient with an acutely infected antrum lies down. The infection must extend rapidly toward the ethmoid and frontal sinuses. Often the patient with an acutely infected antrum complains so bitterly of pain over the frontal sinus that the antrum may be overlooked, even though it is the primary source of infection.

Proetz,[2] Hilding[3] and Tremble[4] have admirably demonstrated the action of the cilia in the antrum about the mouth of the ostium in emptying and directing the flow of secretion away from this cavity. Thus, there is a strong argument for maintaining the antrum wall with its cilia in the region of the middle meatus. It particularly lends force to the condemnation of antrotomies done by way of the middle meatus.

An infected maxillary sinus is most frequently the cause of acute bronchial coughs which persist after what the patient thinks is a common

From the department of otolaryngology, University of Cincinnati College of Medicine.

Presented as a candidate's thesis to the American Laryngological, Rhinological and Otological Society, 1949.

1. Goodyear, H. M.: Use of Iodized Oil in Diagnosis of Nasal Sinus Conditions: Further Observations, J. A. M. A. **95**:1002 (Oct. 4) 1930.

2. Proetz, A. W.: Essays on the Applied Physiology of the Nose, St. Louis, Annals Pub. Co., 1941.

3. Hilding, A. C.: The Physiology of Drainage on Nasal Mucus: III. Experimental Work on the Accessory Sinuses, Am. J. Physiol. **100**:664 (May) 1932.

4. Tremble, G. E.: Clinical Observations on the Movement of Nasal Cilia: An Experimental Study, Laryngoscope **58**:206 (March) 1948.

head cold. It frequently is the source of a persistent afternoon or morning elevation of temperature in a child. I have a patient who spent two years in a tuberculosis sanatorium for a constant cough. Tubercle bacilli were not found. The nose was clean, with a good breathing space. There was no history that roentgenograms of the nasal sinuses had been taken. After two years this young woman left the sanatorium of her own volition. Roentgenograms with iodized oil showed an irregular filling defect in one antrum with some mild clouding of the ethmoid cells on that side. A large opening was made under the inferior turbinate body, and six weeks later the patient stated that the cough had practically disappeared. After eight years there has been no recurrence.

INDICATION FOR SURGICAL INTERVENTION

If it has been determined that an infection of a maxillary sinus is chronic, surgical treatment is indicated. Often the determination of a protracted low grade infection is greatly facilitated by the use of iodized oil as a contrast medium. This is particularly true in the presence of corneal ulcers, infections of the uvular tract, persistent bronchial coughs without pulmonary changes, frequent or persistent colds in children as well as adults, mental depression and even behavior problems in children.[5]

Chronic infection of the maxillary sinus in the presence of allergy adds to the difficulty of decision but does not contraindicate surgical intervention.

CONSIDERATION IN THE CALDWELL-LUC OPERATION

If one determines to open and completely remove a thick infected, cystic, hyperplastic membrane from the antrum, one must do it knowing that nature is not going to reproduce a new and normal membrane. Frequently, repair is by a thick, fibrous membrane sparsely covered with cilia, and unless the opening under the inferior turbinate body is large and remains patent further trouble is usually imminent. When only a large opening under the inferior turbinate body (antrostomy) has been done, a new membrane will also regenerate which may more nearly resemble the membrane of a normal antrum than that developed after a Caldwell-Luc operation and complete removal of the antrum membrane.

When an antrum cavity, which has a normal surface area of some 35 to 50 sq. cm., is completely denuded at one time one is asking a great deal of nature completely to cover this area with normal tissue. Should there be such a denudation of skin in one area, one would surely consider grafting with skin.

5. Goodyear, H. M.: Nasal Sinuses: Practical Considerations of General Interest, J. Med. **13**:528 (Dec.) 1932.

In few cases it is necessary that the maxillary sinus be completely denuded. The success of a radical Caldwell-Luc operation depends not wholly on the complete removal of the membrane but more, as to the final result, on the size, shape and position of the opening under the inferior turbinate body and the care given the patient after operation. If a proper opening is made under the inferior turbinate body, a diseased membrane, which may completely fill the antrum, either recovers or a new membrane regenerates, as has been clearly demonstrated in cases completely filled with hyperplastic membrane recovering following antrostomy with removal of as little of the hyperplastic membrane as possible.[6] It is the opening under the inferior turbinate that is important, not the opening in the canine fossa, nor the complete removal of the antrum membrane.

WHY DO ANTROTOMIES FAIL?

In 1943 a report was made of 100 cases from the New York Eye and Ear Hospital [7] in which operation was done for maxillary sinus infection. in 50 per cent the Caldwell-Luc operation and in 50 per cent intranasal antrotomy. The greatest number of failures followed antrostomy. The authors stated:

> In a large number of cases we found the antrostomy opening quite small and located superiorly, just beneath the attachment of the inferior turbinate, usually quite well posteriorly, and in such a position the aperture certainly does not permit drainage or ventilation. Its purpose has then been defeated. We do not know the cause of our failures.

It is quite clear that the antrotomies were improperly performed, and very little or no relief would have possibly occurred in the chronically infected antrum. In order to succeed, there must be a very large permanent opening under the inferior turbinate for years (usually for life) after operation. Especially must the posterior portion of the opening be wide and well rounded.

The authors of this quotation are not to be criticized. They were following a procedure commonly taught in doing an antrotomy.

An antrotomy operation requires specific instruments and precise procedure throughout. Otherwise, it cannot succeed. One of the arguments for the Caldwell-Luc operation is that it gives a good exposure and a direct route of attack on the ethmoid cells. This is true, but in the performance of the operation the pars membranacea with its cilia is destroyed and the normal ostium of the antrum obliterated.

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6. Goodyear, H. M.: Chronic Antrum Infection: Treatment by Intranasal Antrum Operation and Packing; Clinical and Experimental Results, Arch. Otolaryng. **20**:542 (Oct.) 1934.

7. Stahl, R. H.; Voorhees, D. R., and Davol, R .T.: A Survey of Antral Surgery: Review of One Hundred Cases, Laryngoscope **53**:186 (March) 1943.

Again I wish to emphasize the importance of saving the membrane and middle meatal wall of the antrum. It is in this area that there is the greatest action of the cilia which prevent secretions coming from the region of the frontal sinus or the ethmoid cells from entering into the antrum.

If an infraorbital ethmoid cell is present, it usually appears on roentgenograms as a partition in the upper medial angle of the antrum. This compartment can be reached successfully through the antrotomy by means of a Pratt curet (fig. 1). If the floor of this cell is removed it has had the best of treatment. It is argued that an opening under the inferior turbinate is always above the floor of the antrum which, however, does not seem too bad as to the end result. A small ridge in the lower

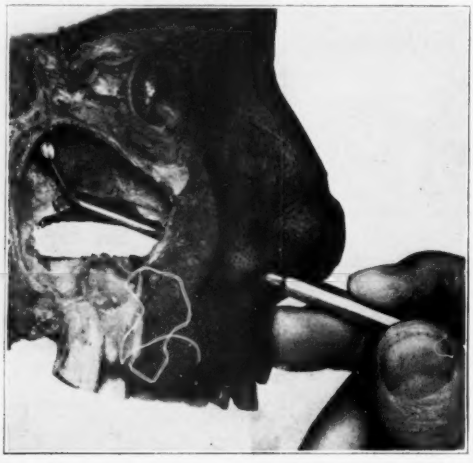

Fig. 1.—Use of the Pratt curet for approaching the naso-orbital angle of the maxillary sinus.

border of the opening helps to keep secretions which are passing backward on the floor of the nose from entering the antrum.

HISTORY

Credit for first advocating approach to the maxillary antrum through the inferior meatus goes to J. Mikulicz,[8] who described his antrotomy in 1886 and voiced his disapproval of Zuckerkandl's[9] approach through the middle meatus.

8. Mikulicz, H.: Zur operativen Behandlung des Empyems der Highmorshöhle, Arch. f. klin. Chir. **34**:626, 1886-1887.

9. Zuckerkandl, E.: Normale und pathologische Anatomie der Nasenhöhle und ihrer pneumatischen Anhänge, Vienna, W. Braumüller, 1893.

Mikulicz' method is of historical importance, but to Lathrop,[10] of Boston, goes the credit for describing in the year 1897 a routine method of enlarging the Mikulicz opening. Unfortunately, in his technic Lathrop sacrificed a portion of the inferior turbinate body.

STEPS IN THE OPERATION

Anesthesia.—A local anesthetic plus 1½ grains (0.1 Gm.) of pentobarbital sodium given orally thirty to forty minutes before operation, preceded by a subcutaneous injection of 1/6 grain (10 mg.) of morphine, combined with 1/150 grain (0.4 mg.) of scopolamine given one to one and a half hours before operation is sufficient.

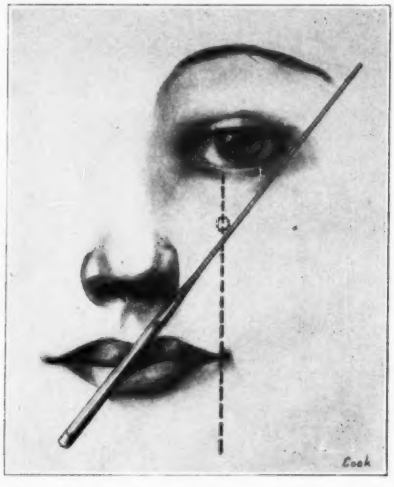

Fig. 2.—Line impressed on the cheek as aid in locating the infraorbital foramen.

A 10 per cent solution of cocaine is applied in the nose to the region of the sphenopalatine ganglion and to the inferior and the middle meatus.

The local injection of 1 per cent procaine hydrochloride into the infraorbital foramen is carefully done in the following manner: After the cheek has been painted with a solution of tincture of merthiolate,® the locating of the foramen is facilitated by pressing a wire applicator firmly against the cheek from the nasolabial fold to the outer canthus of the eye. The injection is then made at the junction of this line (fig. 2), impressed upon the cheek, and an imaginary line in the sagittal plane just medial to the angle of the mouth. Gentle palpation with the fingers may also help to locate the foramen.

10. Lathrop, H. A.: Empyema of the Antrum of Highmore: A New Operation for the Cure of Obstinate Case, Boston M. & S. J. **136**:455 (May) 1897.

An ordinary hypodermic needle (⅝ inch [1.6 cm.]) is inserted into the foramen firmly to the hub, as advocated by Hill,[11] and 1 cc. of the solution is injected slowly.

Infiltration about the foramen will often give very good anesthesia after fifteen to thirty minutes, but injection directly into the foramen is much preferred.

A few drops of procaine hydrochloride is now injected into the anterior area of the nasal septum on the side of operation to prevent unnecessary shock or discomfort of instruments being passed by this area. A small amount of procaine is also injected into the anterior lateral floor of the nose and the anterior attachment of the inferior turbinate body.

The patient is permitted to rest for fifteen minutes between the local injection and the operation.

Position of Patient.—The sitting position (straight upright) is advantageous and the head, with the chin slightly lowered, should be held firmly by an assistant.

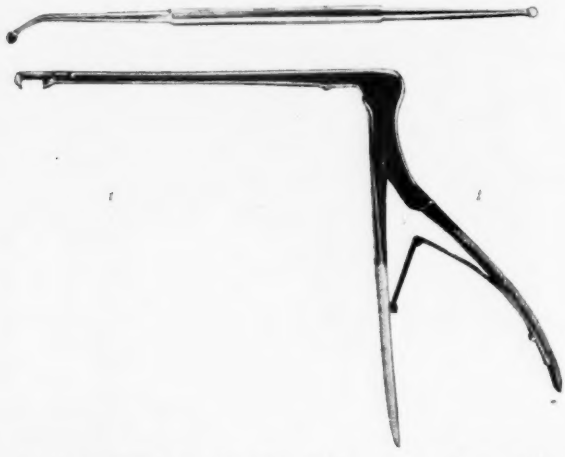

Fig. 3.—Above, Pratt's anterior ethmoid curet; below, heavy Hajek-Kofler downward biting sphenoid forceps.

The stool of the operator should be somewhat higher than the usual working position. Many antrotomies are only partially successful because at operation the chin was not maintained in a lowered position and the operator was not sitting high enough to permit the proper application of the cutting forceps. These are important details for the steps which are to follow.

Elevation of Inferior Turbinate Body.—The inferior turbinate body is elevated by means of the curet end of a Dunning (Carter) submucous elevator placed firmly against the lower edge of the turbinate. Should undue injury occur to the inferior border, annoying synechias may result. If synechias should occur after operation, they should be cut and the turbinate again elevated for a period

11. Hill, F. T.: Local Anesthesia for Surgical Treatment of the Sinuses, Arch. Otolaryng. **127**:197 (Feb.) 1938.

of two weeks; when healing has occurred, the turbinate may again be lowered to its normal position.

Perforation.—Perforation is made with a Bishop perforator and withdrawn with a slight rotation forward, producing sufficient opening for the next step in the operation.

Opening Anteriorly.—A Wagner tip on a universal handle is used to cut anteriorly upward and downward to round the anterior portion of the opening. If

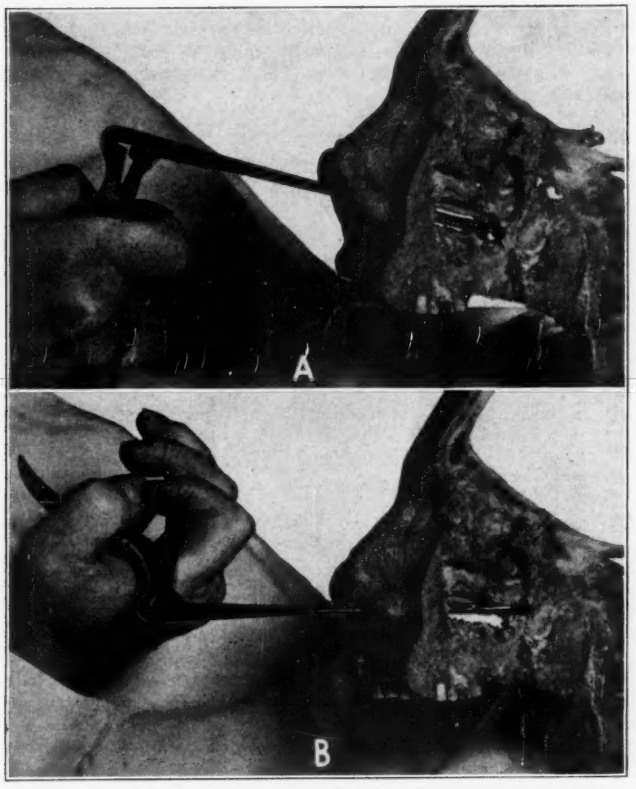

Fig. 4.—*A*, nose pushed well laterally and downward biting sphenoid forceps in proper position for cutting posteriorly and downward. *B*, position of hand and instrument with nose pushed firmly toward the opposite side in rounding the opening superiorly.

the bone is unduly hard, a downward biting sphenoid forceps (Hajek-Kofler) may be used to increase the anterior opening.

Opening Posteriorly.—Here is where most failures in antrotomies occur. Of all the instruments particularly designed for this detail of the operation, none have been adequate.

To determine the effect of various instruments for this procedure I used frozen heads, which were sawed in the sagittal plane in such a manner that the medial wall of the maxillary sinus was preserved and visible. The various instruments were then inserted through the nose and their action observed on the exposed wall of the sinus.

The most satisfactory opening was obtained by the use of a Hajek-Kofler heavy downward and through cutting sphenoid forceps [12] (fig. 3). The tip of this instrument placed on a Universal handle proved unsatisfactory, as did also instruments with a weak or bending shank. Considerable pressure must be applied posteriorly, cutting as far posteriorly as possible and then downward (fig. 4*A*) and upward (Fig. 4*B*), to round out the posterior portion of the opening. The success of an antrotomy depends largely upon the precision and thoroughness exercised in making this portion of the opening.

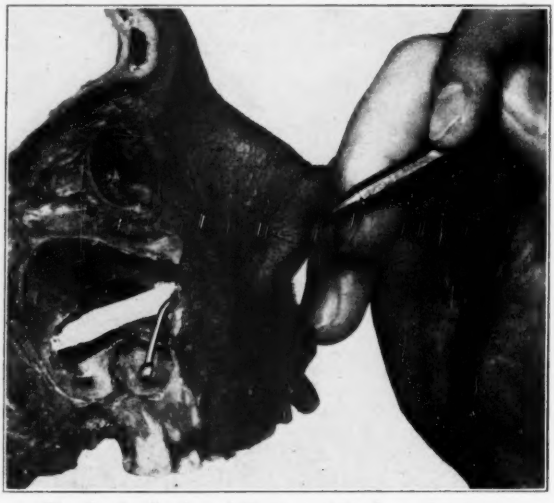

Fig. 5.—Application of Pratt curet to floor of antrum.

Injury to the descending palatine artery has not occurred experimentally or in practice, as the blunt rounded end of the sphenoid forceps protects this vessel. Experimentally a Gruenwald type of forceps will injure this vessel, and in all cases in which severe postoperative bleeding occurred I had used a Gruenwald forceps in extending the antrotomy posteriorly.

Should bleeding occur, packing the antrum and the antrotomy opening is effective. In only 1 of my cases was it necessary to open through the canine fossa to control the bleeding.

Opening Inferiorly.—The sphenoid forceps used in the fourth step of the operation just described may be used to remove the bone toward the floor of the nose, but this edge of the opening can best be finished with the Yankauer downward biting antrum forceps.

12. This forceps is produced by the Storz Instrument Company, St. Louis.

The five steps in performing an antrotomy are now completed: (1) elevation of the inferior turbinate body; (2) perforation; (3) anterior cutting; (4) posterior cutting, and (5) inferior cutting. Each step is distinct and requires a different instrument, except that the sphenoid forceps may be extended, after making the posterior opening, over the lower edge of the antrotomy before finishing with the Yankauer tip on a universal handle.

Dealing with the Antrum Cavity.—A Pratt curet (fig. 3) is passed to the various angles and especially to the nasoantral angle (fig. 1) where occasionally it will be necessary to remove the floor of an infraorbital ethmoid cell which may form a partition in this section of the antrum. Care is exercised not to destroy the pars membranacea as the middle meatus should remain intact.

Gentle curettage of the floor of the antrum (fig. 5) may help to stimulate more rapid regeneration of a diseased membrane, but no attempt is made to denude the antrum cavity completely.

Packing.—Firmly packing the entire maxillary cavity with a continuous strip of ½ inch (1 cm.) iodoform gauze controls bleeding that might occur immediately

Fig. 6.—Applicator with split end for grasping gauze packing.

after operation, and the pressure on a diseased cystic membrane seems to have a beneficial effect on the regeneration and healing of a diseased membrane. Robison [13] has also come to this conclusion. For this reason it is well if the packing remains for four to seven days, or longer if the patient is comfortable. Packing is best accomplished with a straight bayonet forceps.

AFTER-CARE

Removal of Packing.—I have seen surgeons struggle in an attempt to grasp the packing for removal with such instruments as a bayonet or nasal forceps. Often the nose is swollen and tender and the patient is apprehensive. Much discomfort may be avoided in this procedure by the use of a split end applicator (fig. 6) rotated in the gauze packing after an application of a 10 per cent solution of cocaine. This instrument will also be found helpful in destroying a small polypus in the olfactory area or in removing cotton lost in the mouth of the sphenoid sinus.

After removal of the packing the patient is seen within a week or ten days, at which time a 5 per cent solution of cocaine is applied to the antrum cavity and the walls firmly palpated with a wire applicator carrying 2 to 5 per cent solution of silver nitrate on cotton. Should any cysts be present they usually rupture, as indicated by a straw-colored fluid.

13. Robison, J. M.: Application of Local Pressure to the Mucosa of the Maxillary Sinus, Tr. Am. Acad. Ophth. **51**:461 (May-June) 1947.

The applicator is also firmly pressed anteriorly and posteriorly in the antrotomy opening to discourage formation of adhesions.

The patient should be seen at intervals until the antrum wall is smooth and secretion is not obtained on applying a dry cotton applicator to the floor.

SUMMARY

An attempt has been made to show why many antrotomies fail and to stress in detail precisely each step required in a successful operation. It is not an operation to be considered lightly.

Most important, I have introduced not a new but a different instrument, a heavy (Hajek-Kofler) downward biting sphenoid forceps for making the most important—the posterior—part of the antrotomy opening. I have stressed the point of having this instrument on a permanent handle with a very stiff shank and of cutting the opening as far posteriorly as possible.

The importance of iodoform packing is emphasized not only for hemostasis but for the beneficial effect of pressure against a diseased hyperplastic membrane, stimulating more rapid regeneration of a new or healthy membrane.

The importance of retaining the pars membrana intact is distinctly emphasized.

I have described a helpful method of locating the infraorbital foramen and of grasping the packing for removal from the maxilliary sinus.

OZENA

Evaluation of the Surgical Treatment

MATTHEW S. ERSNER, M.D.
AND
MAURICE H. ALEXANDER, M.D.
PHILADELPHIA

EVER SINCE it has been possible to make a diagnosis of atrophic rhinitis with ozena, physicians have sought means whereby this disease may be combated, or at least a treatment which would allay the unpleasant signs and symptoms of the condition. These methods have been basically hygienic, but, except for creating a state of cleanliness, they have been unsatisfactory in control of the disease.

Atrophic rhinitis with ozena tends to attack more than one member of a family and is more prevalent in females than in males. It shows no predilection for Russian Jews or for heavy smokers but is prevalent in the Near East—in Latins and Orientals. Although it is also encountered in the Negroes of the United States, it is not seen in the African Negro.

Atrophic rhinitis with ozena is the end result of an inflammatory disease of the mucosal parenchyma of the nose and the lining of the accessory sinuses and begins in early childhood (fig. 1).

Several postgraduate students from the Near East have informed us that atrophic rhinitis with ozena is one of the common diseases of their country. This may explain why an incense burner is a part of the household equipment of the Near East. Whether the incense combats the odor of the ozena or whether it is a part of the atmosphere of the Near East is debatable.

Through the years there have been many attempts at the medical and surgical treatment of this condition, either by stimulating the surface of the mucous membrane or by narrowing the nasal chambers.

Cauterization of the mucous membrane by use of chemical agents, such as silver nitrate, 5 to 20 per cent, or trichloroacetic acid, 1:2,000, has been tried. Cotton pledgets of McBride's solution,[1] iodides, potassium iodide and various other drugs were also used in attempts to cure this

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1. McBride's solution has the following formula: iodine, 0.5 part; potassium iodide, 1.6 parts; glycerin, 30 parts.

malady, with little or no effect.[1a] Thyroid,[2] vitamins,[3] estrogens[4] and vaccines have had their trial and have been no more successful than efforts to determine the etiology of the disease. It seems that the blood supply of the atrophied mucous membrane is insufficient to produce granulation faster than the denuding effects of the crusting.

As far back as 1919 one of us (M. S. E.)[5] published an article on vaccine therapy of ozena.

The bacteriologic characteristics of Brucella foetida (Coccobacillus foetidus ozenae Perez) were compared with those of Escherichia bronchiseptica and Klebsiella pneumoniae. The Br. bronchiseptica was studied by Perry, McGowan, Torrey and Rahe and was identified by them as being the specific cause of canine distemper and as being morphologically almost identical with, and in many instances biologically similar to, the Perez organism. Burckhardt and Oppikofer placed the organism tentatively among the Aerobacter aerogenes group.[6] Horn placed it with the colon-typhoid bacilli.

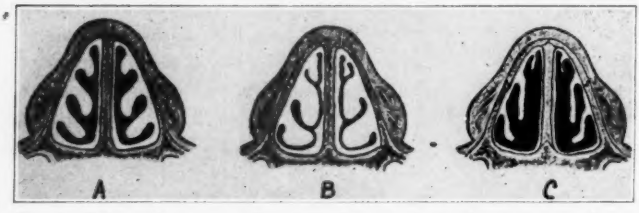

Fig. 1.—Schematic cross section of the intranasal chamber: *A*, normal mucous membrane; *B*, hypertrophic mucous membrane; *C*, atrophic mucous membrane, with increased space.

Attempts have been made to inject paraffin in a semisolid state by stages under the mucous membrane or the mucoperichondrium of the septum and into the structures of the lateral nasal wall. It was then

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1a. (*a*) Naftzger, J. B.: Atrophic Rhinitis: Ozena, Ann. West. Med. & Surg. **1**:18 (March) 1947. (*b*) Lederer, F.: Diseases of the Ear, Nose and Throat, Philadelphia, F. A. Davis Company, 1938.

2. Cullom, M. M.: Ozena, J. A. M. A. **117**:987 (Sept. 20) 1941.

3. Cody, C. C.: Vitamin Therapy in Otolaryngology, Arch. Otolaryng. **41**:208 (March) 1945.

4. Fitzhugh, W. M., Jr.: Atrophic Rhinitis and Ozena, Arch. Otolaryng. **42**:404 (Nov.-Dec.) 1945.

5. Ersner, M. S.: Ozena: Vaccinotherapy; Results of Serologic, Antigenic and Food Anaphylactic, Laryngoscope **29**:22 (Jan.) 1919.

6. Ersner,[5] Thornell, W. C.: Ozena: Bacteriologic and Pathologic Studies, Proc. Staff Meet., Mayo Clin. **21**:90 (Feb. 20) 1946.

suggested that layers of ivory be inserted in an attempt to narrow the nasal passage. The foreign body reactions set up by this method sometimes produced, if they remained in situ at all, a condition as difficult to manage as the atrophic rhinitis. Beck took splinters of bone from the patient's ribs and inserted these, a few at a time, under the mucoperichondrium, the procedure depending on how rapidly the grafts took. This method seemed more logical in view of the improved circulation to the area if the bone graft should take. This procedure had the advantage that, in addition to narrowing of the air passage, the mucous membrane itself retained the power of regeneration. Eisenstodt [7] suggested implantation of cartilage into the nasal septum beneath the mucoperichondrium bilaterally in an effort to narrow the air passage. He actually advocated narrowing the nares to cut down air flow.

More recently, Proud [8] advocated insertion of acrylic transplants submucously between the mucous membrane and the nasal septum to narrow the nasal fossae.

Lautenschläger [9] advocated the operation in which a buccogingival incision was made and the lateral nasal wall was separated along the floor of the nose, starting at the piriform sinus. The wall was then infracted to bring the turbinate bodies closer to the septum. The fragments of bone in the antrum were débrided, with the thought that the initial condition stemmed from chronic sinusitis. The lateral nasal walls were kept in contact with the septum until the bone healed.

Wittmaack [10] modified the Lautenschläger operation by transplanting a buccal fold of mucous membrane, with the opening of the parotid duct, into the maxillary sinuses; thus, the parotid saliva constantly flowed over the walls of the sinus and entered the mouth through a permanent fistula in the buccogingival fold.

Halle [10] further modified this operation into what he called the Halle-Lautenschläger method. As an exponent of the intranasal technic, he made no buccogingival incision, nor did he include a flap of the buccal mucous membrane or the parotid duct in the operation. His technic consisted in a chisel cut along the entire floor of the lateral nasal wall, which sets the nasal wall free from its attachments except at the superior border. The septum and turbinate bodies were then scarified, and the

7. Eisenstodt, L. W.: Surgical Treatment of Atrophic Rhinitis, Arch. Otolaryng. **40**:45 (Dec.) 1944.

8. Proud, G. O.: Acrylic Resin Implant for Atrophic Rhinitis (Preliminary Report), Laryngoscope **57**:256 (April) 1947.

9. Lautenschläger, A.: Operative Behandlung atrophischer Zustände des Naseninnern, Arch. Laryng. u. Rhin. **31**:103, 1918.

10. Kirschner, M.; Lautenschläger, A., and Kleinschmidt, J.: Operative Surgery, translated by I. S. Ravdin and G. M. Coates, Philadelphia, J. B. Lippincott Company, 1937, vol. 3.

entire lateral nasal wall was infracted to bring the scarified surfaces together; they were kept in contact by packing the antrum with gauze until synechias were formed between the turbinate bodies and the septum.

Hinsberg [11] reported a further modification in which light magnesium plates are fastened to the sinal surface of the lateral nasal wall and, with fine magnesium wire, are held in place through the wall, the inferior turbinate body, the septum, the inferior turbinate body on the opposite side, the opposite lateral nasal wall and the second plate. These are then tied in order that pressure may be exerted toward the midline without the antrums having to be packed. The magnesium is resorbed or removed when the lateral nasal wall has been fixed toward the median line. Seifert,[10] using only a suture, devised a similar operation without the magnesium plates.

During the course of performing several hundred rhinoplastic procedures in which the nose was narrowed with or without cancellous bone transplants on the dorsum, we noted that the patients with atrophic rhinitis and pronounced crusting showed specific improvement after the rhinoplasty wound had healed. The procedure of completing an osteotomy during a rhinoplasty had the specific effect of narrowing the air passage of the nasal chamber without distortion of its shape or relative proportions. In addition, when cancellous bone grafts were implanted into the dorsum of the nose, these grafts served to make the chamber narrower, improved circulation to the area and, at the same time, corrected the saddle nose deformity.

In the review of these cases, it was found that virtually all patients with atrophic rhinitis alone or atrophic rhinitis with ozena, particularly the latter, possessed to some degree a saddle deformity of the nose. This deformity, which appeared as a hook or hump, was usually a pseudohump rather than a true hump, because the deformity was caused by dissolution or absorption of the triangular and quadrilateral cartilages, such as it often seen after faulty submucous resection and contraction of the fibroconnective tissue. Thus, it would seem that the procedure should be of distinct benefit to patients with atrophic rhinitis and ozena, not only in narrowing the nasal passage sufficiently to produce relief of symptoms, but also in restoring the cosmetic effect of any concomitant nasal deformity. This operation was performed in 12 cases, with definite beneficial effect.

To perform this operation, one must be thoroughly acquainted with rhinoplastic procedure. The operation in itself does not pose any problems severer than those of any previously devised surgical procedure for ozena.

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11. Lederer, footnote 1a, part *b*. Kirschner and others.[10] Hinsberg, V.: Operative Therapy for Ozena, Monatsschr. f. Ohrenh. **55**:1269, 1921.

In introducing the modified rhinoplastic operation for the treatment of ozena, measures are directed primarily toward the restoration of physiologic function and, at the same time, the production of a cosmetic improvement of the nose. In operation for cosmetic repair the hump is removed and a cancellous bone graft is inserted; thus, the patient has a straight dorsum with the physiologic improvement in the ozena.

TECHNIC

Our operative technic in the treatment of ozena is performed in one stage, providing the disease is not too far advanced:

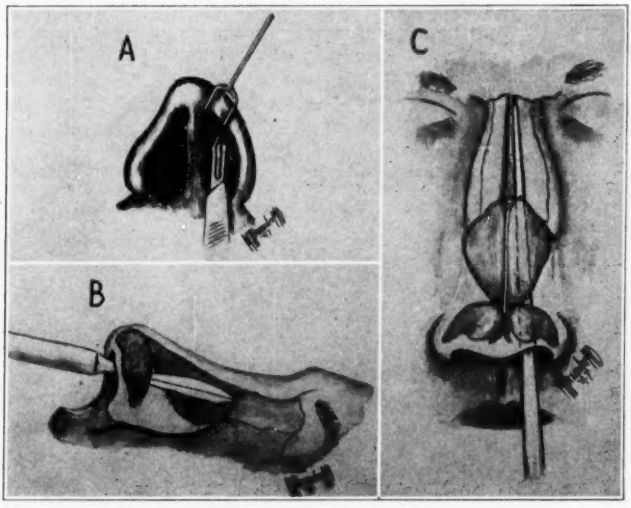

Fig. 2.—*A*, site of incision at caudal end of upper lateral cartilage; *B*, position of Fomon knife in freeing soft tissue over the dorsum of the nose; *C*, method of separating nasal bones from the perpendicular plate of the septum.

1. The patient is placed in a recumbent position, and the face, nasal vestibules and operative area are subjected to a thorough cleansing with soap, water, alcohol and ether, followed by a 1:1,000 colorless merthiolate® solution, a colorless mercury bichloride solution or a 1:1,000 solution of benzal konium (zephiran®) chloride.

2. With regional block anesthesia produced with a 1 per cent procaine solution containing 1:30,000 epinephrine hydrochloride, the anterior palatine, the infratrochlear, the ethmoidal and the infraorbital nerve, with its nasal branches, are anesthetized. It should be noted that in this operation the nasal mucous membrane is not anesthetized, so that the sensitivity of this membrane is retained as a safety measure.

3. With a Bard-Parker knife with a no. 11 blade, an incision is made intranasally, slightly above the caudal border of the upper lateral cartilages within the nose (plica nasi) (fig. 2*A*). The incision is as deeply subcutaneous as possible. As a precautionary measure, in making this intercartilaginous incision, one should be careful not to make more than one incision; otherwise, there will be unnecessary trauma and additional formation of scar tissue.

4. With the double-edged Fomon knife, the incision is carried up over the ventral portion of the nose (dorsum nasi), to and barely beyond the distal border of the nasal bone (fig. 2*B*).

5. The same procedure is repeated on the opposite side of the nose.

6. The periosteum is elevated from the nasal bones along the dorsum, and the nasal bones are then separated from the perpendicular plate of the ethmoid bone with a chisel and mallet in order to break the spring. It must be borne in mind

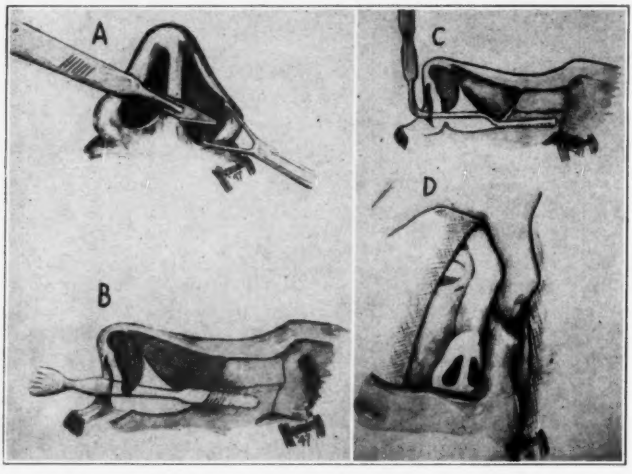

Fig. 3.—*A*, incision of piriform sinus for osteotomy; *B*, elevation of periosteum over the frontal process of the maxilla; *C*, saw in situ for osteotomy; *D*, method of narrowing the nose by infraction.

that with surgical procedures the blood circulation of the external and internal areas of the nose is greatly impaired. Therefore, in separating the nasal bones from the septum, in order to break the spring so as to make it possible to narrow the nose after osteotomy, one should be careful not to disturb the periosteum unduly over the ventral portion of the nose (dorsum nasi) (fig. 2*C*).

7. Another incision is made in the inferior lateral portion of the anterior chamber of the nares exactly at the edge of the nasal process of the maxilla in the piriform process; the point of the scalpel should impinge on the anterior surface of the bone (fig. 3*A*).

8. With the Joseph type of periosteal elevator, the periosteum of the maxilla is elevated along the Gale (nasomalar) groove to the inner canthus of the eye on each side, and the bone is sawed partially through (fig. 3*B*). In

doing the osteotomy, one should be careful not to saw too deeply, and to avoid piercing the mucosa. Otherwise, one is apt to penetrate into the nose and damage the intranasal mucous membrane, which is already partially deprived of its circulation.

9. In creating the nasomaxillary groove, one should avoid cutting through completely, but should cut through sufficiently to create a groove in the frontal process of the maxilla so that a complete fracture will result, with complete immobilization and narrowing of the nose. A complete cut through the bone at this point might endanger the circulation of the mucous membrane by injury to the membrane, and it is for this reason that the inside of the nose is not anesthetized. Thus, if the saw were to penetrate at any point, the warning signal would be acute pain. Every caution should be taken to avoid a greenstick fracture, as such a fracture would result in incomplete narrowing. Both frontal processes are then fractured by application of thumb pressure medially. (figs. 3*C* and 3*D*). A definite snap is heard when the nose is completely fractured and narrowed. A low osteotomy of the frontal process of the maxilla is performed, so that the detached frontal process of the maxilla rests within the nose and close to the nasal septum. This procedure creates an actual narrowing and prevents synechia. When the frontal process of the maxilla rests within the nose, there is also less likelihood of any callus formation (fig. 4).

Fig. 4.—Schematic illustration of diminished space accomplished by osteotomy. *A*, nose before operation; *B*, nasal bones separated and frontal process of the maxilla cut; *C*, new position of the frontal process of the maxilla after osteotomy.

A change in the procedure was undertaken in several cases in which it was thought feasible to separate the upper lateral cartilages and to sew them over the ventral portion of the nose (dorsum nasi), instead of using the bony transplant to fill in the concavity. This modification helped also to narrow the nose and, at the same time, filled in the concavity.

In cases of mild atrophic rhinitis one may also narrow the ala of the nasal vestibule in a one stage operation. But, in cases of more advanced atrophic rhinitis it is best to perform a subsequent operation on the ala so as not to disturb the circulation too much at one time.

At this later stage, when the ala is narrowed so as further to reduce the size of the vestibule the volume and velocity of the air intake are therefore changed. A wide, roomy nose is not necessarily conducive to the proper volume of air intake or to proper distribution of the air. Normally, the nose is provided with upper and lower lateral cartilages, which act as valves, and the elliptic nares act as pressure slits, or chinks, through which the inspired air is forced and distributed. For this reason, wide nares, which are encountered in ozena are frequently narrowed in order to improve the synergistic action of these fluttering valves.

SUMMARY

A modified one stage rhinoplastic procedure for the improvement of atrophic rhinitis with ozena is introduced.

The results of this operative method for the symptomatic improvement of the disease are evaluated.

In a series of 12 patients, surgical procedures produced the following symptomatic relief:

(*a*) Crustation was notably diminished after the rhinoplasty wound had healed.

(*b*) There was restoration of physiologic respiratory function, and several patients noted improvement in their sense of smell.

(*c*) With the low osteotomy, a narrowing of the nasal chamber was actually produced; this, in turn, helped to change the volume and the velocity of the air intake. We wish to emphasize that any defect in the technic of performing the osteotomy will defeat the purpose of the entire operation. Therefore, it is of utmost importance that a low osteotomy be performed in order that the narrowing of the nose be accomplished. Otherwise, the frontal process of the maxilla and the nasal bones will remain gabled, instead of narrowed, and will not be displaced toward the median line.

(*d*) Cancellous bone grafts implanted into the dorsum nasi (ventral portion of the nose) not only served to fill in the concavity but also helped to improve circulation to the nose.

(*e*) In addition to restoration of physiologic function, there was cosmetic improvement in the concomitant nasal deformity.

As a safety measure, the internal nasal mucous membrane is not anesthetized, the sensibility indicating the nearness of the approach of the saw to the mucous membrane in performing the osteotomy.

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TREATMENT OF ALLERGIC AND VASOMOTOR RHINITIS WITH HESPERIDIN CHALCONE SODIUM

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TUCSON, ARIZ.

THE DESIGNATION vitamin P was given in 1936 by Szent-Györgyi and his Hungarian co-workers to a substance or group of substances, other than ascorbic acid, which were present in extracts of paprika and lemon peel. The letter "P" was chosen because the preparation appeared to restore to normal abnormally increased permeability of capillaries.[1] The crystalline extract obtained from lemons was termed "citrin." This extract was believed to contain two different flavone dyes, hesperidin and eriodictyol glucoside, and was said to decrease the number of hemorrhages in scorbutic guinea pigs and to prolong their survival time. Clinical application indicated that the increased capillary permeability associated with nonthrombopenic purpura and infections was corrected by oral administration.[2] Early attempts [3] to confirm the results obtained in animals were unsuccessful, but later several investigators were able to show that vitamin P does

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From the Thomas-Davis Clinic.

Ingram Laboratories Inc., San Francisco, supplied the material used in this study.

Thesis approved by the faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science [M. Sc. (Med.)] for graduate work in otolaryngology.

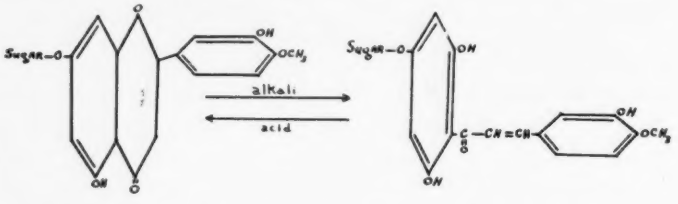
1. Armentano, L.; Bentsáth, A.: Beres, T.; Ruszynák, S., and Szent-Györgyi, A.: The Effect of Substances of the Flavone Group on Capillary Permeability: Vitamin P, Deutsche med. Wchnschr. **62**:1325, 1936.

2. Bruckner, V., and Szent-Györgyi, A.: Chemical Nature of Citrin, Nature, London **138**:1057, 1936.

3. Zilva, S. S.: Vitamin P., Biochem, J. **31**:915; 1488, 1937. Moll, T.: The Question of Vitamin P, Klin. Wchnschr. **16**:1653, 1937. Detrick, L. E.; Dunn, M. S.; McNamara, W. L., and Hubbard, M. E.: Vitamin C Studies: I. The Effect of Vitamin P (Citrin) on Vitamin C Deficient Guinea Pigs, J. Lab. & Clin. Med. **25**:684, 1940. Szent-Györgyi, A.: Methods for the Preparation of Citrin, Ztschr. f. physiol. Chem. **255**:126, 1938. McHenry, E. W., and Perry, H. M.: Observations on the Relation of Vitamin P to Scurvy, J. Nutrition (supp.) **19**:12, 1940.

affect capillary resistance.[4] It was found also that certain flavone dyes caused sudden decreases in blood pressure when administered intravenously, but that hesperidin and eriodictyol did not.[5]

Wawra and Webb,[6] at the University of California Medical School, initially prepared citrin by a method similar to that of Szent-Györgyi, which consisted in extraction of ground lemon peel with acetone, precipitation with barium hydroxide and liberation of the pigment with sulfuric acid in a small volume of methyl alcohol. On the preparation's standing for several days, a white precipitate of hesperidin slowly separated out, accompanied with bleaching of the solution. This observation, along with others in the course of the work, led Wawra and Webb to regard the yellow eriodictyol of Szent-Györgyi as the chalcone of hesperidin. This explains the difficulty encountered by Szent-Györgyi in separating hesperidin from the yellow material, inasmuch as there is an equilibrium between the flavonone and its open chalcone isomer (figure).



Hesperidin (flavanone glycoside)

Hesperidin chalcone
2',3,4',6'-tetrahydroxy-4-methoxychalcone glycoside

Structural formula showing equilibrium between the flavonone and its open chalcone isomer.

The material used in this work is pev-gram,[6,7] which is the sodium salt of hesperidin chalcone. The chemical formula is di to tri sodium salt of 2',3,4',6'-tetrahydroxy-4-methoxychalcone-6-6rhamnoglucosid.e The mechanism of the action of vitamin P is not entirely unknown, but much work has yet to be completed with proper testing for verification. The mode of action as suggested by Lavollay is quite inter-

4. Zacho, C. E.: The Influence of Ascorbic Acid and of Citrin on the Capillary Resistance of Guinea Pigs, Acta path. et microbiol. Scandinav. **16**:144, 1939. Bacharach, A. L.; Coates, M. E., and Middleton, T. R.: A Biological Test for Vitamin P Activity, Biochem. J. **36**:407, 1942. Bourne, G. H.: Vitamin P Deficiency in Guinea Pigs, Nature, London **152**:659, 1943.

5. Armentano and others.[1] Bruckner and Szent-Györgyi.[2]

6. Wawra, C. Z., and Webb, J. L.: Isolation of New Oxidation-Reduction Enzyme from Lemon Peel (Vitamin P), Science **96**:302 (Sept. 25) 1942.

7. Pev-gram, registered trade name of Ingram Laboratories, Inc., San Francisco, for hesperidin chalcone sodium.

esting: Vitamin P acts as an inhibitor of an oxidizing enzyme—amine oxidase—and thus inhibits the oxidation of epinephrine. This action explains why favorable results are obtained in the treatment of vasomotor and allergic rhinitis, because epinephrine is a natural antagonist to histamine.

The nose, besides constituting the natural airway for respiration, has three primary functions: (1) It accommodates the olfactory organ; (2) it conditions the inspired air to the requirements of the pulmonary surfaces by warming, moistening and filtering it, and (3) it cleanses itself of the foreign material which it has extracted from the air. This last-named function, completely overlooked by most authors, is at least as important as the rest for health and much more important than the rest in the control and eradication of infectious diseases and pollens. Other attributes ascribed to the nose, such as vocal resonance, gas exchange and the regulation of air flow, are secondary and usually incidental.[7a]

The term "allergy" was coined by von Pirquet to denote a state of altered reactivity on contact with foreign substances. The term has been generally accepted as applying to all the forms of hypersensitiveness in man, such as asthma, allergic rhinitis (hay fever), vasomotor rhinitis, eczema, urticaria and migraine. By modern definition allergy is a state of exaggerated susceptibility to a foreign substance or physical agent that is harmless to the majority of people.

Hay fever is an allergic nasal syndrome occurring seasonably and produced by hypersensitization to the pollen of plants when the pollen is in the air. Vasomotor rhinitis is a constantly recurring or chronic and persistent form of nasal allergy, usually due to hypersensitization to inhalants, food, bacterial protein or to any combination of these. Between acute attacks of hay fever, or allergic rhinitis, the nasal mucous membrane may often show this vasomotor type of reaction.

The chief pathologic change in the nasal mucosa is edema. The epithelium is edematous, with desquamation of cilia and cells and an increase in goblet cells; the basement membrane may be thin or thickened. The changes in the tunica propria are most characteristic and consist in edema, which begins and is most pronounced in the subepithelial layer of the mucosa, while the deeper layers are less swollen. In addition, there is eosinophilic infiltration, with increase of lymphocytes, plasma cells and fibroblasts. When the connective tissue of the tunica propria can no longer support the weight of the edema, it prolapses as a mucous or edematous polyp. Where the connective tissue is

7a. Proetz, A. W.: Physiology of the Nose, in Jackson, C., and Jackson, C. L.: Diseases of the Nose, Throat, and Ear. Philadelphia, W. B. Saunders Company, 1945.

firmer, as on the septum, the inferior turbinate bone and the medial surface of the middle turbinate bone, sessile masses, called polypoid hyperplasias, form.[8]

The treatment of allergic and vasomotor conditions of the nasal passages has gone through numerous phases and changes during recent years. Many new remedies which are considered superior to older drugs are always appearing in the literature, but to date we physicians are still looking for more relief for our patients. The product pevgram® was used in the study presented here to determine its effectiveness in the relief of symptoms resulting from rhinitis of the allergic and vasomotor types. Ninety-nine patients were studied, and the work was continued over a period of approximately eighteen months. The ages ranged from 14 to 65 years. The conditions treated ranged from severe edematous allergic rhinitis, showing pronounced eosinophilia on examination of nasal smears, to mild nasal stuffiness, with no infection or eosinophilia on examination of nasal secretions.

Incidence of Relief from Symptoms with Use of Hesperidin Chalcone Sodium

Type of Rhinitis	Complete Relief	Partial Relief	No Relief	Side Reactions
Severe edematous allergic	0	6	16	2
Mild to moderate seasonal allergic	5	11	3	1
Vasomotor	28	17	6	2
Vasomotor, with associated migraine headache (histamine cephalalgia)	2	..	..	..
Total number of patients	35	34	25	5
Per cent	35	34	25	5

This group of patients lived on the desert in the Southwest at the time this study was made. However, many of them came from practically every part of the United States, with a few from Canada and Mexico. Due to the mild climate here, there are pollens in the air approximately ten months out of each year. For this reason the duration of the seasonal types of hay fever is greatly prolonged. Besides this, the always present house dust must be considered. The dust of the desert is practically inert, but it does cause a certain amount of irritation of the nasal mucous membrane, which, added to nasal sensitivity, aggravates the symptoms.

Another factor that causes trouble is the physical type of vasomotor rhinitis. This condition is due to extreme changes in climatic temperature. On the desert, the change in temperature is as much as 40 to 50 degrees daily. Most patients had trouble adjusting from the warm to

8. Morrison, W. W.: Diseases of the Nose, Throat and Ear, Philadelphia, W. B. Saunders Company, 1938.

the cool air, but a few had just the opposite problem. The relative humidity, which is low on the desert, augments the physical reaction of the nasal mucosa. In the table is shown the response obtained with hesperidin chalcone sodium.

Thirty-five patients, or approximately 35 per cent, showed complete relief from symptoms. None of the patients with severe edematous rhinitis showing eosinophilia of the nasal secretions had complete relief from symptoms. Five patients with a pale-looking mucous membrane, associated with seasonal sneezing and nasal stuffiness, responded satisfactorily. Twenty-eight patients with a vasomotor type of nasal mucous membrane had complete relief from symptoms. Two patients with vasomotor rhinitis, associated with a migraine type of headache, experienced complete relief from the nasal symptoms and the headaches.

Thirty-four patients, or approximately 34 per cent, had partial relief from symptoms. Six patients with the severe edematous type of allergic rhinitis had partial relief from symptoms, but further therapy was necessary to obtain satisfactory relief. Eleven patients with the seasonal type of allergic rhinitis of a mild to moderate degree had partial relief from symptoms. Four of these 11 patients were sufficiently comfortable so that further study and therapy were unnecessary. The 7 remaining patients required additional study before sufficient relief was obtained. Seventeen patients with the vasomotor type of reaction had partial relief from symptoms. All but 2 of these patients obtained sufficient relief so that further therapy was limited to the use of mild nose drops for occasional nasal stuffiness. Twenty-five, or approximately 25 per cent, of the patients obtained no relief from the use of hesperidin chalcone sodium.

Sixteen patients had the severe edematous type of allergic rhinitis; 3 patients had mild to moderate seasonal allergic rhinitis, and 6 patients, the vasomotor type.

Side reactions were noted in 5 patients, or approximately 5 per cent. Two of these patients had the severe type of rhinitis: 1, the mild to moderate type, and 2, the vasomotor type. Two patients had hives (urticaria) within twenty-four hours after the therapy was started. One patient with bronchial asthma experienced pronounced aggravation of the asthma, and the drug had to be discontinued. The 2 other patients experienced nausea without vomiting, which may or may not have been a direct result of the drug.

The use of hesperidin chalcone sodium had not eliminated or reduced the incidence of nasal surgery. The patients with nasal polypi required polypectomy. Patients with deviation of the nasal septum required submucus resection. When indicated, partial middle turbinectomy, formation of antral windows and similar nasal surgical procedures were done before relief from the use of the drug was experienced.

REPORT OF CASES

CASE 2.—M. S., a white woman aged 28, had severe seasonal hay fever due to fall ragweed at her home in Indiana. The remainder of the year she was fairly comfortable but always susceptible to infections of the upper respiratory tract. She had moved to Arizona in 1942 and had been comfortable and had no nasal troubles for two years. Nasal stuffiness with postnasal drainage occurred and became increasingly worse. Skin testing showed that the patient was moderately sensitive to bermuda grass, mesquite and dust. Examination of the nose showed an allergic type of mucous membrane during severe attacks and a vasomotor type of mucous membrane between acute flare-ups. Pev-gram® gave her the first real relief from the symptoms. It required 200 to 300 mg. of hesperidin chalcone sodium daily to control them. After the symptoms subsided, 100 to 150 mg. daily, in divided doses, was sufficient to maintain relief.

CASE 3.—T. M., a white woman, aged 35, complained of nasal stuffiness associated with deafness in the right ear. Examination revealed vasomotor rhinitis with moderate conduction deafness on the right side. Treatment with pev-gram® was started, 150 mg. being administered daily, in divided doses. The nasal stuffiness subsided, but the conduction deafness persisted. Catheterization of the right eustachian tube on several occasions improved the loss of hearing. Later, while still continuing this therapy, the patient complained of nasal stuffiness. Examination revealed the airway to be large and widely open bilaterally. The therapy was changed, but she continued to complain of nasal stuffiness regardless of the fact that the examination usually revealed an adequate airway bilaterally.

CASE 42.—S. H., a white woman aged 24, complained of headache, stuffy nose, postnasal drainage and sneezing. Examination showed an allergic rhinitis not complicated with infection. Nasal smears showed an elevation in infiltration of eosinophils. Skin testing indicated a sensitivity to bermuda grass and rabbit bush. Besides this, she was decidedly allergic to eggs, which when eaten would cause an asthmatic attack to occur immediately. The patient was unable to eat away from home because of this extreme allergy to eggs. She was advised to avoid eggs completely, and treatment with hesperidin chalcone sodium was started; 400 mg. were required daily, in divided doses, to relieve the symptoms. After they were relieved, the dose was gradually decreased until the patient was being maintained on 150 mg. daily, in divided doses.

CASE 52.—L. L., a white woman aged 65, had had severe attacks of dizziness associated with nasal stuffiness, headache and nausea for the past ten years. These attacks were of such severity that she had to remain in bed for from twenty-four to seventy-two hours at a time. Her home had been in New York, where she had frequent infections of the upper respiratory tract. These infections always aggravated the attacks. Examination revealed vasomotor rhinitis with moderate conduction deafness bilaterally. The results of the examination otherwise indicated nothing abnormal. The patient was given 200 mg. of hesperidin chalcone sodium daily, in divided doses. She has experienced only an occasional headache since the therapy was started and no attacks of dizziness sufficient to require her to be in bed. At present, she is taking 150 mg. daily and has started to work again, which she had not done for several years because of this disability. This therapy left the deafness unchanged, and the patient is now planning to purchase a hearing aid.

CASE 69.—H. J., a white man aged 42, had symptoms of sudden dizziness which caused him to wreck his car. He would fall when walking, and one such attack resulted in lacerations of the face. There were no prodromal symptoms which

would indicate such violent dizziness, and accidents, therefore, could not be avoided. Examination showed vasomotor rhinitis. Results of examination of the ears, nose and throat were completely negative otherwise. The systolic blood pressure was 128; the diastolic, 84. The patient had been seen in Michigan for these same attacks and was given large doses of ammonium chloride orally, which gave partial relief for a relatively short time; but the severe attacks recurred even while this therapy was being used. The results of skin tests with histamine were positive. Desensitization with histamine diphosphate was not sufficient to control the attacks. Desensitization, together with the use of 200 mg. of hesperidin chalcone sodium daily, in divided doses, gave complete relief from attacks. At present, he receives a maintenance dose of 100 mg. daily, in divided doses, and has had no attacks for more than eight months. One mild attack which occurred was associated with too many cocktails the previous evening.

CASE 80.—W. R., a white man aged 40, came to me with a diagnosis of histamine cephalalgia. His symptoms were severe headaches associated with nasal stuffiness and postnasal drainage, lasting for approximately six weeks and recurring two or three times yearly. Examination at the time of attacks showed a severe vasomotor rhinitis with considerable increase in mucus drainage. No pus was demonstrated, and roentgenograms of the sinuses indicated nothing abnormal. He has a septum-turbinate body adhesion on the right side, but this does not bother him except during attacks. These attacks completely incapacitate him. Desensitization with histamine gave only partial relief from symptoms. Treatment with hesperidin chalcone sodium, 200 mg. administered in divided doses, was started in association with histamine desensitization, and the patient has had no debilitating attacks for more than fourteen months. At present, he receives a maintenance dose of 100 mg. daily, in divided doses.

CASE 96.—B. S., a white man aged 33, complained of nasal stuffiness, sneezing and postnasal drainage. Examination showed vasomotor rhinitis. Skin testing showed a 4 plus allergy to bermuda grass. Several other products for oral administration were used to control the symptoms, but these products caused drowsiness, with dryness and itching of the nose. Treatment with pev-gram® was started. It required 200 to 250 mg. daily, in divided doses, to control the nasal symptoms, but the side reactions of drowsiness, dryness and itching were not experienced.

The dosage of pev-gram® varied, depending on the severity of the symptoms. The average dose was 3 capsules, or 150 mg., daily, of hesperidin chalcone sodium. In all cases in which relief was experienced, a larger initial dose was required. This dose varied from 300 to 400 mg. daily, over a period of from two to five days. As soon as relief from the symptoms occurred, the daily doses were gradually reduced, and a maintenance dose of 100 to 150 mg. daily was sufficient to control the nasal symptoms. In the severe allergic cases which did not respond, daily doses of 400 to 600 mg. were given. It was felt that greater amounts would not give relief, so the drug was discontinued.

The length of action of pev-gram® is approximately four to six hours, with recurrence of symptoms in about six to eight hours. When the drug is withdrawn, the symptoms reappear, except in those cases in which the offending material was removed or when the patient's allergic state had temporarily subsided.

SUMMARY

Hesperidin chalcone sodium has gained most of its popularity in maintaining normal capillary permeability and in correcting decreased capillary resistance. However, Lavollay has suggested that the action occurs because vitamin P is an inhibitor of an oxidizing enzyme—amine oxidase—and inhibits the oxidation of epinephrine. This explains why favorable results are obtained in the treatment of allergic and vasomotor rhinitis, because epinephrine is a natural antagonist to histamine.

Hesperidin chalcone sodium was used in the treatment of 99 patients with allergic and vasomotor rhinitis. Thirty-five per cent of the patients obtained complete relief from symptoms, 34 per cent obtained partial relief and 25 per cent experienced no relief. Five per cent of the patients showed side reactions: urticaria, aggravation of bronchial asthma and nausea without vomiting.

The amount of hesperidin chalcone sodium required for relief varied from 100 to 600 mg. daily, in divided doses. The duration of action is over a period of four to six hours, and the symptoms reappear if the drug is withdrawn unless the offending factors are removed or the allergic state has passed.

The incidence of nasal surgery has not been affected by this therapy.

130 South Scott Street.

MODIFIED TECHNIC OF PLASTIC PROCEDURE IN RADICAL MASTOIDECTOMY

Report of Results in a Case of Circumscribed Labyrinthitis and Periphlebitis of the Lateral Sinus in the Course of Chronic Purulent Otitis Media with Cholesteatoma

WALTER DWORETZKY, M.D.
NEW YORK

UNTIL the advent of such powerful antibiotics as penicillin, streptomycin and aureomycin, surgeons did not dare after a radical mastoidectomy to cover entirely with a plastic skin flap a labyrinthine fistula or periphlebitic bony defect of the lateral sinus, caused by active chronic purulent mastoiditis.

In the case described here such a procedure combined with the use of antibiotics applied to both these lesions gave an excellent result and speeded healing.

REPORT OF CASE

S. S., a student at New York University aged 31, was first examined by me on Dec. 16, 1948. He complained of recurring discharge from the right ear since early childhood and deafness on this side. For the last several months prior to the examination, spells of dizziness appeared, accompanied with nausea, especially on sudden and rapid movements.

Otoscopy of the right ear revealed a large granulation polyp in the bony part of the external meatus and a moderate amount of very foul purulent discharge containing white pearly flakes of cholesteatoma. The results of the Bezold test were positive. The left ear was normal.

Anterior rhinoscopy showed deviation of the septum to the right in its cartilagenous and bony parts, with subluxation into the left nostril. There was moderate secondary hypertrophy of the left lower turbinate bone. Both nasal cavities were obstructed, the right considerably more. Posterior rhinoscopy showed a slight enlargement of the posterior poles of the lower turbinate bodies. The pharynx was injected. In the right ear whisper was heard at the concha. The results of the Rinne test were negative. In the Weber test sound lateralized to the right.

In the accompanying audiogram are shown the results of the audiometric examination. The solid (preoperative) audiometric curve shows the average loss of air conduction hearing of the right ear for the frequencies in the speech range to have been about 65 decibels, with the loss for the 1024 frequency as low as 70 decibels; for high tones, the average loss was 85 decibels. The dotted curve expresses bone conduction hearing of the right ear. The broken line indicates air conduction hearing of the right ear seven weeks after the operation (February 21), showing an average improvement of about 10 decibels. The solid line (with x's) expresses air conduction of the left ear.

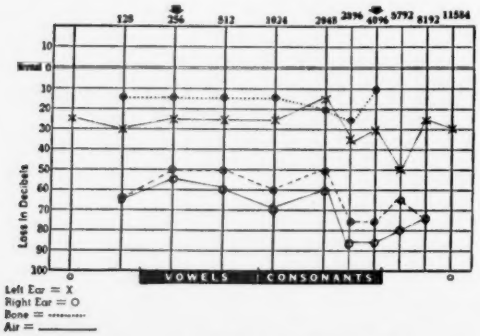


Fig. 1.—Audiogram made on Dec. 17, 1948.

Fig. 2.—Roentgenograms showing (*A*) normal left mastoid and (*B*) sclerotic right mastoid.

Spontaneous nystagmus of second degree to the left was noticed. The reaction to the fistula test was strongly positive: The tip of the index finger pushed against the outer meatus caused such a vigorous reaction that the patient had to be prevented from falling and a jerky nystagmus of third degree to the right persisted for about three minutes.

The roentgenographic examination of both mastoid processes was reported by Dr. Arthur Ettinger as follows: The left mastoid is normal. In the right mastoid the antrum is densely sclerotic, and there is an absence of cellular structure in the posterior portion of the mastoid. The roentgenographic characteristics indicate chronic mastoiditis on the right side.

A radical mastoidectomy by postauricular approach was performed on Jan. 4, 1949, with general anesthesia. The following conditions were encountered: The mastoid process was sclerotic, long and narrow, and corresponded to the elongated skull of the patient. A few small periantral and perisinal cells and the tip cell

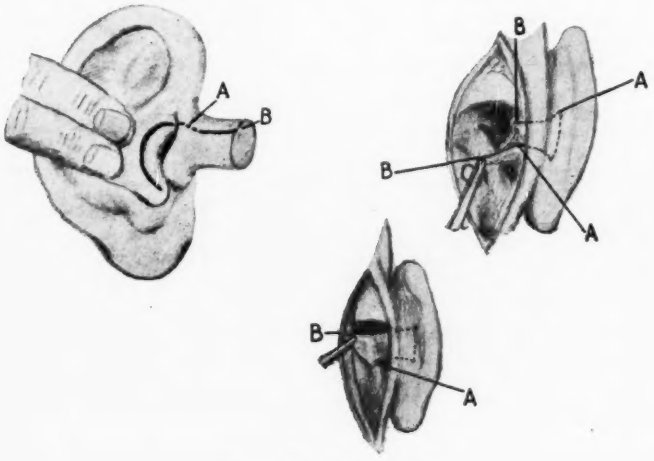


Fig. 3.—Operative technic.

were filled with pus and granulations. The antrum and the epitympanum were packed with cholesteatoma; the incus and malleus were missing. Beneath the dry inner surface of the matrix of the cholesteatoma, the mesial bony wall appeared polished. The prominence of the lateral semicircular canal was flattened, and a slitlike fistula without any granulations was evident in the canal. The lateral sinus was located too anteriorly—a quite common finding in a narrow mastoid process. The bony plate of the sinus was eroded; the erosion, of an irregular outline, was approximately the size of a dime. The sinus wall proper in this spot was discolored and thickened. The sinus was exposed around the defect in its bony plate beyond the area of the periphlebitic changes but was not punctured because the patient had none of the symptoms before the operation suggestive of obstructing thrombosis or thrombophlebitis (the temperature had been normal, and there had been no headache or chills, etc.). After the removal of the cholesteatoma and other pathologic tissues and the thorough eradication of all changed

cells, the radical mastoidectomy was completed, the tympanic cavity scrupulously cleaned, the bony part of the eustachian tube curetted and a modified plastic procedure performed.

The plastic procedure is described in detail as follows:

The success of the plastic procedure in radical mastoidectomy is appraised by a smooth, complete and durable epidermization of the whole wound inside and by a good cosmetic effect outside, behind the auricle, in the postauricular method.

To reach this goal, the plastic operation was performed in a way which permitted diminishing the area for epidermization to the limit and fully utilizing the meatal skin for a flap. The conventional postauricular incision in its upper three fourths ran alongside and slightly behind the hair line and in the lower one fourth curved to the tip of the mastoid process. The meatal flap was formed by two incisions: The first, resembling Lempert's endaural incision, followed the edge of the auricular cartilage, with the starting point at the anterior-superior wall inward from the incisura anterior (fig. 3, upper, left). The second *(AB)* incision was carried out from the same point at the right angle to the first one, straight mesialward to the inner end of the external canal (fig. 3, upper, right). The angle *B* of the meatal flap thus formed by these incisions was stitched to the inner surface

Blood Counts

Date	Erythrocytes, No.	Hemoglobin, per Cent	Leukocytes, No.	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Eosinophils, per Cent	Basophils, per Cent
1/6	4,310,000	84	21,200	70	27	3	..
1/10	4,670,000	90	13,900	70	22	6	2
1/14	4,843,000	90	11,650	62	34	2	2
1/19	4,270,000	80	10,500	50	36	14	..

of the posterior postauricular flap as far backward as possible from the latter's edge and above the level of the lateral semicircular canal. The meatal flap, somewhat overstretched, loosened considerably after the closure of the postauricular opening and thus was easily adjusted to cover entirely the labyrinthine fistula and the defect in the sinus (fig. 3, lower illustration).

Such an arrangement of the plastic flap diminished considerably the area left for epidermization (above the meatal flap) and shortened greatly the healing period. The cavity below the flap, formed after the postauricular incision was sutured, readily filled with blood. Caution was exercised while the wound was dressed to avoid pressure on this slightly bulged area and thus promote healing by "the blood clot method." The inside dressing, consisting of several strips of petrolatum gauze, was packed tighter in order to insure the proper adherence of the meatal flap to the covered area.

The postoperative course was as follows: The day of the operation and the following day passed without any distressing symptoms, except for slight dizziness and nausea. Two days preoperatively and two weeks postoperatively, the patient was given sulfonamide drugs by mouth and 300,000 units of procaine penicillin in oil intramuscularly daily. From the morning of January 6 till the morning of January 12, the patient exhibited the signs of "destruction disharmony" (induced labyrinthitis): fits of dizziness accompanied with nausea, vomiting and strong spontaneous nystagmus of third degree to the left. The most frequent and severest fits occurred on January 8, 9 and 10, when the patient could hardly retain food.

On January 9 the dressing was loosened inside; on January 12 the stitches were removed and the whole dressing changed. Until January 15 inclusive, the dressing was changed every day, and afterward, every second day. After January 13 the patient did not vomit, but during several days he still experienced dizziness and nausea from time to time. The lively spontaneous nystagmus of third degree to the left, which persisted from January 6 to January 12, changed into a slower nystagmus of second degree. All these symptoms gradually improved. The first three days after the operation the temperature did not exceed 101.6 F., and afterward it was below 100 F. The high leukocyte count (21,200) gradually dropped to normal. The urinalysis did not reveal any abnormalities.

On January 18 the patient was allowed to walk, at the beginning with the nurse's help. After January 19 all medications, including sedatives, were discontinued. On January 26 the patient was discharged from the hospital in good condition, with the wound almost healed. The wound was dressed every second day at my office, and after the seventh dressing, the postoperative care was considered finished. The epidermization of the operative cavity was complete. The

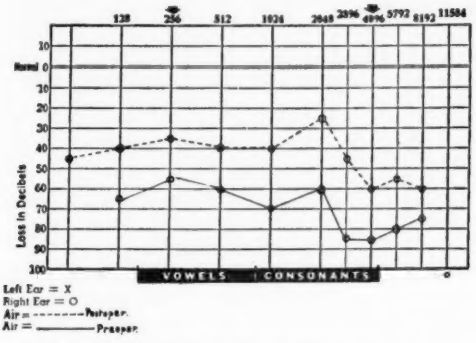


Fig. 4.—Audiogram made on March 17, 1949.

cosmetic appearance of the postauricular area was excellent: Its shape did not differ from the contour of the side not operated on, and the scar was almost indistinguishable. On February 13, five weeks and three days after the operation, the patient, with my consent, attended his sister's wedding party, drank alcohol and danced till early in the morning without any ill effect.

The patient was presented on February 21 at the clinical conference of the Bronx Eye and Ear Infirmary. On March 17, ten weeks after the operation, the right ear was tested again, and the audiogram showed further considerable improvement (fig. 4). The average improvement for the speech range was from 20 to 25 decibels; for 1024 frequency, 30 decibels, and for 2048 frequency, 35 decibels. Whisper was heard at 6 to 7 feet (1.8 to 2.1 meters).

SUMMARY

1. Operative procedure and postoperative care in a case of circumscribed labyrinthitis and periphlebitis of the lateral sinus, in the course of chronic purulent otitis media with cholesteatoma, are discussed.

2. The devised plastic technic made possible the covering of the labyrinthine fistula and the bony defect of the lateral sinus with the meatal flap and diminishing the area for epidermization.

3. This modified plastic flap applied in combination with antibiotics considerably shortened postoperative healing and gave an excellent cosmetic result.

4. In addition to these advantages of this plastic procedure, a noticeable improvement in hearing (from 20 to 35 decibels) was achieved. It remains to be seen whether this improvement will progress and be permanent. It is also too early to judge, ten weeks after the operation, whether the preexisting cholesteatoma will play some role in preventing osteogenesis in the fistula. For this reason the patient should remain under observation, and his hearing should be tested periodically during the next two years.

545 West End Avenue.

Case Reports

SUPPURATIVE SIALADENITIS PRODUCED BY A FOREIGN BODY IN THE HYPOPHARYNX

Report of an Unusual Case

LIEUTENANT COLONEL NORMAN E. KING
MEDICAL CORPS, UNITED STATES ARMY

The case to be reported is unique in my experience, and I am unable to find any such case to date reported in the literature. Furthermore, I am unable to explain the chain of events leading to involvement of the submaxillary glands. Whether the foreign body first entered Wharton's duct and then penetrated to the tonsillar fossa, or whether it entered the peritonsillar area, thus setting up an inflammatory process which dissected through to the gland, is a point of controversy. In view of the history of the case, the latter explanation is the more plausible.

REPORT OF CASE

A man aged 26, a lieutenant in the United States Army, was first seen at an overseas station in June 1945 with the complaint of a prickling sensation in the left tonsillar area. At this time nothing could be seen or felt on examination. A few weeks later he noticed a swelling in the left side of his neck; he experienced considerable difficulty in swallowing, and was unable to open his mouth more than 1 cm. He reported again to his battalion aid station in Germany, where he was given symptomatic treatment for one week, with subsidence of the swelling and pain and relief of the trismus. However, he still noticed a "hard lump" under the left side of the mandible in the region of the submaxillary gland. This lump remained stationary, without producing symptoms, until November, when there developed a simultaneous pronounced swelling under the left side of the mandible, pain in the throat and inability to swallow. The patient reported to a field hospital in Austria, where he was placed under treatment with heat; the symptoms and swelling gradually subsided within fifteen days.

In January 1946 he was admitted to an evacuation hospital with recurrence of the swelling under the mandible, pain on swallowing and some increase in temperature. At this time he was placed under treatment with penicillin and sulfadiazine, and his symptoms subsided within seventeen days.

During each hospitalization roentgenograms were taken, and at no time could calculi or an opaque foreign body be demonstrated.

On January 17, about three days after his discharge from the evacuation hospital, he was readmitted with a rather sudden recurrence of the symptoms and pain in the left ear. At this time a peritonsillar abscess was incised and a moderate amount of pus liberated. He was then placed under treatment with potassium iodide and penicillin, after which his symptoms rapidly subsided.

On February 3 he was returned to the Zone of the Interior for discharge. At the separation center, a physical examination revealed that the tonsils were moderately enlarged, that there was moderate injection of the soft palate on the left and that an old scar was present over the upper pole of the tonsil through which pus was exuding. There was a pedunculated granulating mass in the floor of the mouth on the left over Wharton's duct at its midportion. The left submaxillary gland was enlarged and hard, and pus could be expressed through the duct. Because of these findings, the patient was hospitalized for further treatment and disposition.

Roentgenograms of the gland showed no evidence of calculi. An injection of iodized oil U. S. P. (lipiodol®) into Wharton's duct at this time showed a small amount of oil extending along a narrow tract posterior to the gland and pocketing in the soft tissues at the angle of the jaw. The gland itself was not outlined.

On March 26 a tonsillectomy was performed, and the small granulating mass on the floor of the mouth was removed for biopsy. The pathologic report was returned with a diagnosis of plasma cell granuloma. After removal of the mass, pressure on the gland caused pus to exude from the biopsy site.

The patient was then transferred to an Army general hospital, where the following notation was made: "At present, the left submaxillary gland is definitely enlarged, but it is neither tense nor tender. It feels somewhat cystic and does not appear to be involved in an active inflammatory process. The duct appears normal. There is no bulging into the floor of the mouth or evidence of any remnant of the granuloma which was previously removed. The left side of the soft palate is definitely edematous and intensely reddened. The site of the old incision made in January is still slightly apparent, although there is now no active drainage at this site."

On April 30 a second tonsillectomy was performed on the left side, and the following comment was made: "The left tonsillar fossa and faucial region were greatly indurated, with adhesions. There was a small amount of tonsillar tissue at the lower pole. The whole tonsillar fossa was opened; the tonsillar tissue was removed, and the adhesions were eradicated. When pressure was applied to the left submaxillary gland, secretion was seen to exude from the tonsillar fossa, indicating an apparent direct communication from the gland to the fossa." The pathologic report on the specimen follows: "The specimen consists of edematous granulation tissue, which contains a moderate number of histiocytes and a larger number of lymphocytes and is covered by fibrinous material. In the fibrinous layer is a large number of polymorphonuclear leukocytes and in some areas an accumulation of bacteria. Otherwise, no characteristic details are to be noted." The diagnosis was subacuate inflammatory tissue.

The patient was then placed under treatment with penicillin, 30,000 units being administered every three hours intramuscularly, and received a total of 1,680,000 units.

During the entire postoperative course, pressure on the submaxillary gland produced drainage of creamy yellow pus from the middle of the left tonsillar fossa and from Wharton's duct. On April 26 a smear revealed rare pus cells. Hemolytic streptococci were isolated on culture.

The patient was transferred to the Oliver General Hospital in July 1946, and the following comment was made: "The left submaxillary gland was moderately enlarged, hard and indurated throughout. There was no tenderness. Pressure over the gland caused expulsion of a few small clumps of pus from Wharton's duct; at the same time a small amount of yellowish material exuded from the left tonsillar fossa. The fossa was extremely scarred and fibrotic throughout."

The patient was placed under conservative therapy consisting of administration of penicillin, treatment with heat and daily massage for two weeks and was then given a convalescent leave of thirty days. He was seen again in September, with no change in the physical findings. The results of all laboratory tests were within normal limits. Injection of iodized oil U. S. P. through the sinus opening in the left tonsillar fossa revealed a sinus tract contiguous with the left submaxillary gland and Wharton's duct. Injection of methylene blue through the same opening, after roentgenographic examination, revealed that the dye was expelled freely at the frenulum of the tongue, thus demonstrating a free and continuous communication.

Because of these findings and the patient's history of prolonged illness, a two stage surgical procedure was decided on in which the posterior sinus tract would be excised up to the submaxillary gland, this excision to be followed by extirpation of the gland and duct at a later date.

On October 28, with local anesthesia, a circular incision was made around the sinus tract in the left tonsillar fossa. With the guidance of a probe in the sinus, the dissection was continued laterally and downward to the anterior portion of the posterior belly of the digastric muscle. At this point a pocket, with an approximate diameter of 1 cm., was entered and from it a bristle, identical with an ordinary toothbrush bristle, was removed. The pocket was curetted thoroughly, and the tissues were closed tightly with 00 chromic sutures, without a drain.

The foreign body and the excised sinus tract were forwarded to the pathologist, who made the following report: "Gross examination: Specimen A consists of a piece of apparently vegetable fibrin, measuring 1.5 cm. in length and 0.2 cm. in diameter. Specimen B consists of a piece of tissue of greenish blue discoloration, its surface covered with grayish yellow exudate. Microscopic study: The surface is covered with orderly stratified squamous epithelium of mucous membrane type. In one portion there is moderate acanthosis, but the basal layer is orderly in arrangement, and on one portion of the surface there is a small amount of keratohyaline material. In the underlying stroma there are numerous infiltrating plasma cells and lymphocytes. The sinus tract extends down into the granulating fibrous tissue, which in some areas is undergoing moderate hyalinization, while in others it is infiltrated with lymphocytic accumulations. Throughout the tissue are scattered, rather diffusely, well preserved erythrocytes, which are in areas occupied by adipose cells. At the bottom of the sinus tract, which is not lined with any epithelium, are portions of epithelial rests and salivary glands of mucous type. A few fibers of striated muscle, which are partially hyalinized, remain. The diagnosis is that of a sinus tract showing chronic granulation and inflammation from a foreign body (andropogen scoparius)."

The patient made an uneventful postoperative recovery and on the tenth postoperative day was given a second convalescent leave of thirty days. On his return, it was seen that the tonsillar fossa had healed completely and that the submaxillary gland had returned to its normal size and consistency. No pus could be expelled from Wharton's duct, and the patient was free from symptoms. He was discharged on December 31.

SUMMARY

A case is presented in which a foreign body, a toothbrush bristle, had apparently entered the left peritonsillar fossa and dissected laterally into the neck, setting up an inflammatory process which extended anteriorly to the submaxillary gland and duct and produced sialadenitis and a through and through sinus tract extending from the tonsillar fossa to the frenulum of the tongue.

HYPOPHARYNGEAL POLYP

DAVID W. BREWER, M.D.
SYRACUSE, N. Y.

Polyps involving the hypopharynx are of sufficiently infrequent occurrence to make even a single case of interest.

REPORT OF A CASE

A white woman aged 55 was first seen on Nov. 30, 1948, with the chief complaint of intermittent episodes of nausea, associated with the feeling of a moving lump in the throat. This had been evident during the previous two years but had

Fig. 1.—Roentgenogram showing the mass in the esophagus. The polyp extended approximately 18 cm. down the esophagus to just below the arch of the aorta.

become more noticeable during the past year, particularly during the two months prior to examination. Except for thyroidectomy performed eight years previously, the history was noncontributory.

On two occasions a long, thick, red object was regurgitated and hung out of the mouth down to the chin. The most recent occurrence was one week prior to her examination; at that time, on attempting to close her teeth on the object, she noted that it had the consistency of rubber.

Initial examination showed that the ears, nose and throat were normal. However, after a wait of approximately five minutes, a second indirect laryngoscopy revealed a small, rounded polypoid mass lying in the left piriform sinus. Roentgenographic examination with a barium swallow was performed on the same day. The roentgenologist, Dr. Clayton Hale, reported a smooth, elongated, sausage-like filling defect in the upper half of the esophagus (fig. 1). This soft tissue mass apparently arose near the region of the cricopharyngeal muscle and extended down the esophagus for a distance of approximately 18 cm., or just below the arch of the aorta. There was no evidence of ulceration of any portion of the esophagus, and the mass was therefore considered to be a benign lesion. The hypopharynx and esophagus were otherwise not remarkable.

The next morning, direct laryngoscopy was performed, and approximately 1.5 cm. of the polyp was teased upward; the mass was seen to be attached by a broad base to the left side of the hypopharynx on its posterior wall. Immediately after this, with the patient under anesthesia produced by intravenous injection of thiopental sodium U. S. P. (pentothal sodium®) and with a Brown-Davis mouth

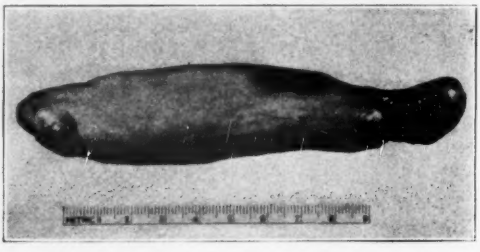


Fig. 2.—Appearance of the polyp after removal. It measured 13.5 cm. in length and 3 cm. in diameter in its midportion.

gag, a proximal portion of the polyp was visualized, grasped and teased upward and an 8 inch (20 cm.) polyp was delivered through the mouth. A tenaculum, through a polyp snare, was placed on the distal end of the polyp, which was lying outside the mouth, and the polyp was removed with the snare. There was a small area of bleeding, 0.5 by 1 cm., in the lower portion of the piriform sinus on the left. Two plain 000 surgical gut sutures were used to approximate the edges of the bleeding area, and the bleeding was controlled entirely by this procedure. The postoperative course was uneventful; the nausea did not recur, and the patient has been asymptomatic since removal of the polyp.

The pathologic report described the polyp grossly as consisting of a huge, polypoid-appearing mass of very soft tissue. It measured 13.5 cm. in length and 3 cm. in diameter in its midportion (fig. 2). It was 2 cm. in diameter at the pedicle. Its surfaces were glistening, whitish pink and smooth in contour. A cross section revealed a fairly well defined outer margin with a very gelatinous, almost myxomatous, tissue in its central portion, which was glassy to whitish in color. The microscopic diagnosis was benign fibromatous polyp.

1100 East Genesee Street.

Clinical Notes; New Instruments and Technics

LINEAR FENESTRATION OF LATERAL SEMICIRCULAR CANAL USING CURETS AND DENTAL EXCAVATORS

ERIC GUTTERIDGE, M.D., F.R.C.S.(Edin.), F.R.A.C.S.
MELBOURNE, AUSTRALIA

The lateral semicircular canal is exposed and skeletalized to the posterior canal, where the curve has a direction directly medialward.

The bony canal is curetted with a Lempert 0000 curet on the cranial, lateral and inferior aspects. With the largest Ash excavator the bony canal is removed down to the facial canal and forward to the vestibule. The blue line of the membranous canal is exposed from the superior canal and followed backward until it disappears from view toward the posterior canal. The excavator hollows the bony wall above and below the blue line. Further curettage removes the outer bony wall of the membranous canal. The excavator enters the canal and removes the overhanging edges until the maximum width is obtained. The smallest excavator has a diameter equal to that of the canal. Bone scrapings are wiped from the excavator and the field is flooded at intervals. The canal is followed to the vestibule and the superior canal may be exposed. The endosteum, presenting as a white lining of the bony fissure, is removed with the needle from behind forward and floated off by irrigation. The ampulla becomes visible, and the endosteum of the vestibule is removed.

It is believed that the bone debris produced by the dental drill is the cause of bone regeneration and closure of the fenestra. The dental excavators, moving away from the membranous canal, collect their scrapings on the disk of the tool, and the debris is wiped off between strokes. It is noteworthy that in the last year of operating, in which the dental drill has been discarded, the incidence of loss of improvement in hearing has become considerably reduced.

The photograph of a dissection of the medial wall of the antrum, attic and middle ear shows the extent of the canal fenestra from the vestibule to the posterior canal, the width obtained and the projection of the bony canal in the center of the fenestra (fig. 1).

Complete removal of the white endosteum is essential; all shreds and streamers are lifted with the handled needle, assisted by gentle irrigation and scraped off against the bony edge of the fenestra. The completed window is of a red shade in its entirety, with, on occasions, the ampulla and membranous canal discernible.

The Ash excavators (fig. 2) have blades 1, 2 and 3 mm. in diameter, respectively. The angle of set of the blades aids in removing the hard bone quickly and permits of direct vision during their action. The blunt rounded edge cannot injure the endosteum and may be inserted into the canal to remove the overhanging rim. The elbow of the instrument permits of a direct approach to the canal being made.

12 Collins Street.

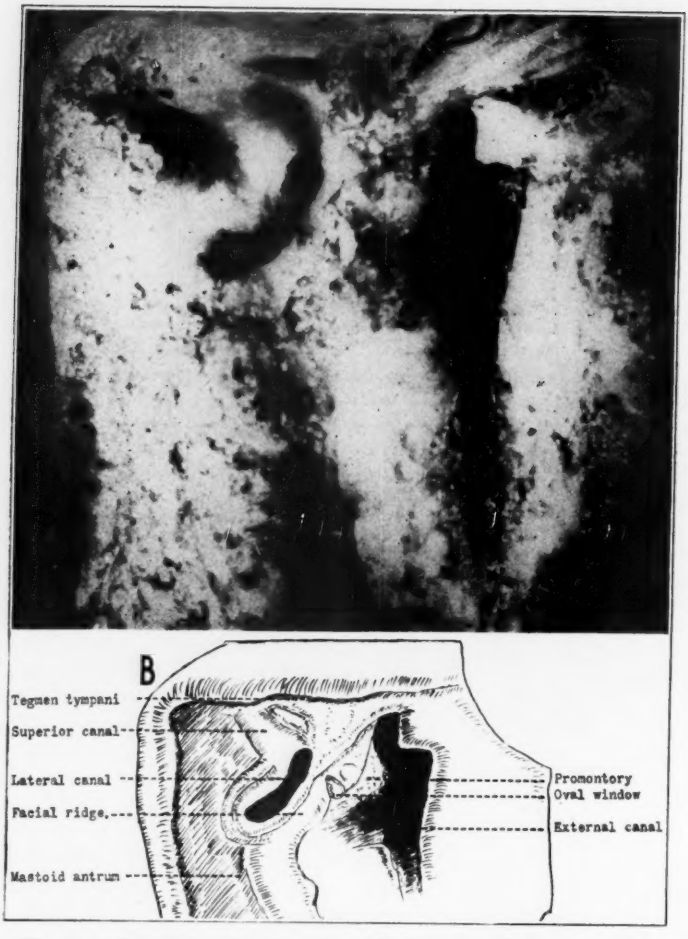


Fig. 1.—*A*, fenestration of the lateral semicircular canal. *B*, diagrammatic key.

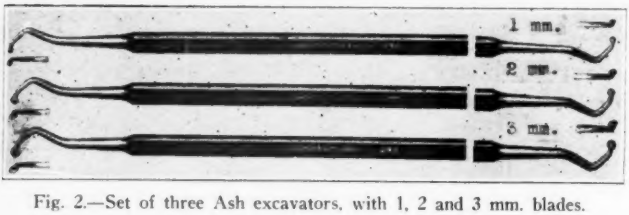
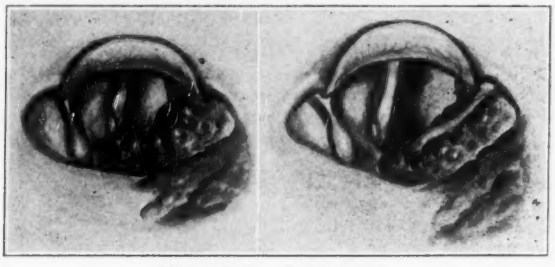


Fig. 2.—Set of three Ash excavators, with 1, 2 and 3 mm. blades.

HEMANGIOMA OF THE LARYNX

H. BERNHARDT, M.D.
TEL-AVIV, ISRAEL

Recently I found among some of the material which I had brought with me from Germany the two accompanying pictures from a case of hemangioma of the larynx, which, so far as I am aware, is quite unique.



Hemangioma of the larynx.

A laborer, aged 35, was referred to me by a general practitioner for relief from severe attacks of suffocation. Examination revealed laryngeal hemangiomas of such size that they could completely obstruct the airway when they were swollen. On the advice of Professor von Eicken, I injected a few drops of 1:1,000 mercury bichloride solution. The effect was rapid. The hemangiomas disappeared completely, and so far as I know there was no recurrence. The patient did not return for further treatment, and he was soon lost to follow-up.

Abstracts from Current Literature

Ear

DEGENERATION AND NECROSIS OF NEURONES IN EIGHTH CRANIAL NUCLEI CAUSED BY STREPTOMYCIN. LEWIS D. STEVENSON, ELLSWORTH C. ALVORD JR. and JAMES W. CORRELL, Proc. Soc. Exper. Biol. & Med. **65**:86 (May) 1947.

Neuropathologic study was made on 5 patients with tuberculosis who had acquired partial or complete deafness while receiving large amounts of streptomycin. Changes were present in the neurons of the ventral cochlear nuclei in all of them. Streptomycin in comparable dosage was administered to 3 dogs, which showed ataxia, tail chasing, weaving of the head and weakness, but disturbance in auditory acuity could not be demonstrated. Liquefaction necrosis was found bilaterally in the ventral cochlear nuclei hence the changes would seem to account for the deafness and vestibular dysfunction in clinical cases.

HANSEN, Galveston, Texas [Am. J. Dis. Child.].

LATENT OTITIS MEDIA IN INFANTS. JEAN DESCAZEAUX, Rev. de laryng. **67**:489 (Sept.) 1947.

Otitis media still is often not diagnosed in time in the presence of gastro-intestinal cholera-like toxicosis resulting from otitic infection. Paracentesis of the drum is performed too late and too seldom in infants.

The diagnosis is frequently not easy: The infant's drum is much more horizontal than the adult's; the pars flaccida is pinkish and occupies a much larger portion of the drum; the short process of the malleus is extremely prominent, and the hammer handle is poorly seen because of the obliquity of the drum. Dulness of the drum with whitish or yellowish discoloration, absence of the cone of light and, sometimes, a "frosted" appearance indicate otitis media. The otoscopic examination should be repeated after several hours to observe the changes in the drum; the paracentesis should include the pars flaccida; if necessary, one should aspirate with Siegle's speculum. Often paracentesis should be bilateral. If no improvement in the symptoms occurs in forty-eight hours, antrotomy is indicated. The author states that he is against the diagnostic puncture of the antrum. Twenty-one cases recorded since 1945 are reported.

HERSON, Chicago.

AURAL DISEASES OF INFANTS. E. GYÖRGY, Paediat. danub. **2**:160 (Aug.-Sept.) 1947.

In the first part of the article several aural diseases of infants, as catarrh of the tube and of the mucous membrane of the tympanic cavity, are discussed. Their symptoms can be divided into otologic (local) and pediatric (general) ones. Methods of medical and the eventual surgical treatment of each condition are dealt with separately.

Otitis is a common disease in the newborn. Its frequency amounts, according to statistical data, to 5 per cent. Its symptoms are enumerated in detail and the author underlines the significance of the sequelae such conditions may have.

Otitis of infants with desquamative erythroderma (Leiner's disease) is dealt with extensively. Differentiation of this condition is necessary as, because of the increased sensitivity and secretion of the skin of the external auditory canal and

of the epidermis of the drum, its pathogenesis varies from that of common otitis. In addition to this, the resistance of such patients is always decreased.

In the last paragraph, symptoms of initial otitis and mastoiditis are enumerated according to their pathogenetic and physiologic aspects. Then propagation of the infection from the tympanic cavity to the cells of the mastoidal process and the pathologic changes of purulent mastoiditis are discussed.

FROM THE AUTHOR'S SUMMARY [Am. J. Dis. Child.].

ROENTGENOLOGIC DIAGNOSIS OF MASTOIDITIS IN INFANTS AND CHILDREN. P. SONNAUER, Paediat. danub. **2**:147 (Aug.-Sept.) 1947.

Three roentgenologic methods are in use in pediatric otology, those of Schüller, Stenvers and Mayer. By their aid it is possible to gather information about the condition of the pneumatic system, the extent of pathologic processes and the site of both the sigmoid sinus and the tegmen. Density of the mastoid cells and destruction of those of the pneumatic system are invariably present with inflammation.

For comparison, bilateral roentgenograms should be made in every instance—every second or third day in acute processes and once a week when the condition is chronic.

In infants, the procedures of Schüller or Mayer are to be used because that of Stenvers presents insurmountable technical difficulties. According to the author's experience, it is possible to gage the density of the antrums in quite young infants, while in those older than 6 months of age even mastoiditis can be seen, as at this age mastoidal cells already show distinct outlines.

FROM THE AUTHOR'S SUMMARY [Am. J. Dis. Child.].

THE SURGICAL PROBLEM IN OTOSCLEROSIS. MAURICE SOURDILLE, Rev. de larynx. **68**:481 (Oct.) 1947.

The author traces the history of the fenestration operation: Holmgren first employed the Gullstrand loupe and the binocular microscope and used radical mastoidectomy; the author himself used partial radical mastoidectomy; Ledoux (1933) used subcutaneous atticotomy, or simple resection of the roof of the auditory canal and the outer wall of the aditus. The latter procedure was later improved by De Lima and Aubry in France.

The author has continued to use the postauricular incision 3 cm. behind the groove; this location of the incision tends to prevent subsequent stenosis of the external canal, which occurs more easily when the incision is made directly in the postauricular groove. After elevation of the skin and the periosteum and performance of a partial radical mastoidectomy with careful removal of the mastoid cells, he performs a tight closure of the tympanic cavity and the attic with a membranous-periosteal flap hinged at the tympanic membrane; this is the same technic used by the author in 1929. To fill the bottom of the mastoidectomy wound, the author uses additional posterior superior and posterior inferior fibromuscular grafts.

HERSON, Chicago.

Pharynx

INFECTION OF THE NECK AFTER TONSILLECTOMY. CLIFFORD F. LAKE, Minnesota Med. **30**:851 (Aug.) 1947.

Infection of the neck after tonsillectomy is not a common occurrence but it does take place, and the author warns that after every tonsillectomy it should be watched for. The situation may be represented by cervical adenitis, cellulitis of

the neck, infection of a fascial space, thrombophlebitis and septicemia or any combination of these conditions. Some of these infections are dangerous and demand prompt rational treatment. In the paper such treatment is given in detail, and in the conclusion the statement is made that tonsillectomy should not be carried out in the presence of acute infection in the pharynx or mouth.

STOESSER, Minneapolis [Am. J. Dis. Child.].

Larynx

FOREIGN BODIES IN THE RESPIRATORY TRACT. JOHN R. RICHARDSON, New England J. Med. **235**:707 (Nov. 14) 1946.

The diagnosis of a foreign body in the respiratory tract is easy when one remembers to think of the possibility. The story of the patient or that of the patient's family should be believed until proved wrong. Roentgenologic examination should include the entire respiratory and digestive tracts. Fluoroscopy of the chest is indicated when a nonradiopaque foreign body is suspected. Unless a foreign body can be completely visualized, it is dangerous for one to attempt its extraction. The safe removal of a foreign body is aided by reference to a duplicate, as well as roentgenologic study, so that its exact position and location are understood. Only then can removal be accomplished without the possibility of doing more harm than good through unwise manipulation.

FROM THE AUTHOR'S SUMMARY [Am. J. Dis. Child.].

ELECTIVE TRACHEOTOMY FOLLOWING THYROIDECTOMY. BERNARD J. FICARRA, New York State J. Med. **48**:919 (April 15) 1948.

This case report is from the Department of Surgery, St. Peter's Hospital, Brooklyn. A man of 56 had hoarseness and dyspnea on exertion for several weeks, associated with a thyroid gland "twelve times normal size." Total thyroidectomy was done, plus an "elective tracheotomy." The tube was removed on the second day, and recovery was uneventful. Compression of the recurrent nerves is common in such cases; edema of the larynx or trachea is the indication for tracheotomy. The hazards of tracheotomy are infection of the wound, emphysema and pulmonary infection. Therefore, penicillin (20,000 units in 1 cc. of isotonic sodium chloride solution five times daily) should be given while the tube is in situ. The best way to prevent emphysema is to pack the wound wide open. Against pulmonary infection, frequent suction and instillation of penicillin through the tube are helpful measures. Prior to removal of the tube, a roentgenogram of the chest should be taken; it may show fluid or an old blood clot. A friction rub similar to a pericardial rub may help to reveal the clot. Tolerance of a stylet in the tube for twelve hours indicates extubation. Three days is the longest time the tube is required.

VOORHEES, New York.

Miscellaneous

THE TREATMENT OF MENINGITIS DUE TO HAEMOPHILUS INFLUENZAE WITH STREPTOMYCIN. LOUIS WEINSTEIN, New England J. Med. **235**:101 (July 25) 1946.

Nine patients with purulent meningitis, due to type B Hemophilus influenzae in 7 and to an untypable strain in 2, were treated with streptomycin, with complete recovery in 7 cases. The drug was given intramuscularly in doses ranging from 15,000 to 125,000 units every three hours and intrathecally in amounts varying

from 10,000 to 25,000 units every twenty-four hours. Two of the 9 patients with influenzal meningitis treated with streptomycin died. One showed complete absence of response to the antibiotic agent. The other died of an intercurrent bronchopneumonia due to Staphylococcus aureus, which was not affected by penicillin.

The blood and spinal fluid were cleared of the causative organisms in from twenty-four to forty-eight hours in all cases except the 2 due to atypical strains. No relapses or sequelae of the influenzal meningitis were observed in any of the recovered patients over a period of from six to ten weeks after the cessation of streptomycin treatment. No toxic reactions attributable to streptomycin were observed in the nervous, hematopoietic or urinary systems.

Infection with Staph. aureus developed in 2 of the patients receiving streptomycin—meningitis in 1 patient and bronchopneumonia in the other—after they had been completely free of H. influenzae in both the spinal fluid and blood for several days and were apparently recovering clinically. Bacteremia was present in both.

FROM THE AUTHOR'S SUMMARY [Am. J. Dis. Child.].

FULMINATING MENINGITIS AND INTRATHECAL PENICILLIN. BYRON D. ST. JOHN, New York State J. Med. **47:** 2603 (Dec. 1) 1947.

A white woman of 23 became violently ill and went quickly into coma, having had symptoms of an ordinary cold. On admission to the hospital, the patient had been ill only about five hours. Spinal puncture showed a pressure of 44 mm. of mercury; there were 13,700 white blood cells, mostly polymorphonuclear leukocytes, per cubic millimeter. No organisms were reported in the smear or the culture. One hundred thousand units of penicillin in 5 cc. of spinal fluid were injected slowly into the spinal canal, requiring forty-five minutes. A violent reaction of the unconscious patient made restraint necessary. Five grams of sulfadiazine sodium were given intravenously at once and 2 Gm. of sulfadiazine through an intranasal tube every four hours. The blood culture remained negative, and there were no organisms in the spinal fluid. Great improvement was noted on the third day, but a severe headache occurred on the fourth day. Spinal puncture was again done, and 8 cc. of opalescent fluid was removed. On the sixth day, the patient's temperature was normal and all medication was discontinued. No nystagmus, squint or double vision were present; the neck was not stiff. One week later, the patient went home, apparently well. She remained in good health to the time of writing, becoming pregnant six months after the illness.

[ABSTRACTER'S NOTE.—It is unfortunate that the germ causing the condition was not found. Apparently this was not a meningococcic meningitis. The author mentions streptomycin as gaining importance in the treatment of meningitis but does not say that he has used it.]

VOORHEES, New York.

ON ORIGINAL WORK IN PLASTIC SURGERY IN NEW YORK STATE. ELIOTT B. HAGUE, New York State J. Med. **48:**617 (March 15) 1948.

This is a historical sketch of the early work in plastic and reconstructive surgery in New York state. For the period prior to the Civil War there is "no record" up to the time of Dr. Frank Hastings Hamilton (1813-1886). Most of the article is given over to eulogy of Hamilton's life and work. He was graduated from the University of Pennsylvania School of Medicine in 1835, became Professor of Surgery in the College of Physicians and Surgeons of Western New York and later held a like position in Geneva Medical College. He is said to have been a "master of . . . extirpative and reconstructive surgery." He evolved the principle of attaching skin grafts to periosteum to avoid retraction

(this principle was the basis of successful plastic surgery about the eye as carried on by the late Dr. John M. Wheeler). Hamilton performed rhinoplasty by the Indian method of transplantation of forehead flaps. In 1858, he extirpated the entire parotid gland; the effect on the facial nerve is not stated. When Dr. Holmes needed support for his theory of the cause of puerperal fever, Hastings "defended (it) with his pen." Hague concludes that reconstructive surgery was advanced by regional surgeons (specializing in pelvic, abdominal or traumatic surgery, etc.) and that much of this work will remain in their hands. There are many competent general and regional plastic surgeons.

(ABSTRACTER'S NOTE.—A strange omission concerns the remarkable work of the late Dr. John O. Roe, of Rochester, who flourished around the turn of the nineteenth century. He was a master in his day and "set" many technics now in use.)

VOORHEES, New York.

A SIMPLIFIED METHOD OF OBLITERATING FRONTAL BONE DEFECTS. D. M. LIERLE and W. C. HUFFMAN, Laryngoscope **59**:61 (Jan.) 1949.

There are many ways to obliterate a bony defect of the skull by transplantation of tissue. Lierle and Huffman fill the cavity with small pieces of autogenous bone. The graft takes well, the shape can easily be molded, and no harm results to the underlying brain tissue.

HITSCHLER, Philadelphia.

POTENTIAL HAZARDS FROM RADIATION TREATMENT OF HYPERTROPHIED LYMPHOID TISSUE IN THE NASOPHARYNX. LAURENCE L. ROBBINS and MILFORD D. SCHULZ, Laryngoscope **59**:147 (Feb.) 1949.

Untoward effects of roentgen ray and radium treatment may not appear for years. Not enough time has passed since the widespread use of the nasopharyngeal radium applicator to be certain that such effects will not appear in the future. Harm has resulted from even an erythema dose, and this dose in some cases is less than that used in the nasopharynx. Furthermore, it is difficult to determine the exact amount of radiation which reaches the tissues from the applicator. Because of these potential dangers, the operator is warned not to use this means of therapy without due consideration.

HITSCHLER, Philadelphia.

THE USE OF SPLENIC EXTRACTS IN THE TREATMENT OF ALLERGIC CONDITIONS OF THE UPPER RESPIRATORY TRACT AND OF BRONCHIAL ASTHMA. VIRGILIO SANGIOVANNI, Pract. oto-rhino-laryng. **9**:79, 1947.

The author presents a report on a series of 20 patients suffering from bronchial asthma and vasomotor rhinitis who were treated with endosplenina® (Istituto-Sieroterapico Milanese), a proprietary extract of the spleen. The course of treatment consisted of a series of five intramuscular injections of 10 cc. each, one given every other day. The results were excellent in 95 per cent of the patients and good in 5 per cent. The asthmatic and nasal disturbances disappeared for periods of from one to four months. In 1 case, there was complete involution of the nasal polyps. Although recurrences did occur, a second or third series of injections produced rapidly favorable results. The author states the belief that the spleen exerts an endocrine influence and that allergic diseases are connected with hormonal imbalance, which may be reduced to a normal state by the administration of splenic extract.

PERSKY, Philadelphia.

Book Reviews

Die Klinik der Labyrinthitis und Paralabyrinthitis auf Grund des Roentgenbefundes. By Prof. Dr. Med. Horst Wullstein, Chief of the Ear, Nose and Throat Department of the Jung-Stilling Hospital, Siegen, Westphalia, Germany. Paper. Price, $8.50. Pp. 150, with 64 illustrations. Stuttgart: Georg Thieme, Verlag. Imported by Grune & Stratton, Inc., New York, 1948.

This book deals essentially with roentgen interpretation of pathologic processes of the internal ear. The first section treats of the methods of examination, in which Wullstein stresses the Stenvers position as being most favorable for accurate interpretation of otic pathologic conditions. While tomographs may be of value in a number of instances, the author relies on the Stenvers position for more exact delineation and structural changes. He states, however, that in spite of the most careful technic, certain conditions cannot be diagnosed with certainty. These are either a small circumscribed area of internal otitis or a diffuse internal otitis, involving only the mucosa of the inner ear. Other conditions involving the destruction of the bony capsule can readily be diagnosed, particularly when there is frank osteitis.

The second section deals with roentgen findings and, in many instances, with photomicrographs of many pathologic conditions. The roentgenograms are clarified by schematic drawings, which explain the condition present. The author begins this section by presenting the normal structures and proceeds with the discussion of many pathologic conditions, such as cholesteatoma and erosion of the various sites throughout the inner ear. The various disorders are illustrated by actual case histories, in which the entire course of the disease is briefly outlined.

The third section of the book is concerned essentially with symptomatology, diagnosis and treatment. Considerable emphasis is placed on the role of chemotherapy. Included is an extensive bibliography. The book, although confined to an extremely narrow field of otology, presents the newer thoughts on the subject of diagnosis and treatment of labyrinthitis and is of a considerable value both to the otologist and the roentgenologist.

Radiologic Exploration of the Bronchus. By S. di Rienzo, M.D., assistant professor of Radiology and Physiotherapy; Chief of the Radiology Department of the Institute of Cancer, University of Cordoba, Argentina. Translated by Tomas A. Hughes, M.D., with a foreword by Richard H. Overholt, M.D. Price, $10.75. Pp. 346, with 520 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1949.

This new work concerning the bronchus is devoted, as the title indicates, to the radiologic exploration of the tracheobronchial tree and pulmonary segments for clinical diagnostic and therapeutic aspects. The author is well qualified to present this material, which is well organized, rather clearly written and logically presented.

Numerous references at the end of each chapter supplement the material from the author's own experience in this field. The book is adequately illustrated, even though some illustrations are used as many as three times throughout the text. There are thirteen chapters in the book on embryology of the respiratory

tract, bronchial histology, anatomy of the bronchus, bronchographic characteristics of the normal bronchus, radiologic exploration of the bronchus by the contrast method, tomography, serial exploration, bronchopulmonary malformations, bronchiectasis, emphysema and asthma, carcinoma of the lung, hydatid cyst of the lung and suppuration. The book is completed by an index of authors, subjects and illustrations. This work should be of interest to clinicians, roentgenologists, otolaryngologists and thoracic surgeons in particular.

Rienzo has had many years of clinical experience with the subject he discusses, and for this reason the book merits some consideration. For example, a fine comparison of the various classifications of bronchial branches is contained for the reader's information. In passing, an exception may be taken to the statement that accidents nearly always occur with the use of contrast substances. With the measures used by most of the large clinics in this country, this is the exception rather than the rule.

Reconstructive and Reparative Surgery. By Hans May, M.D., F.A.C.S., Assistant Professor of Surgery, Graduate School of Medicine, University of Pennsylvania. Foreword by James Barrett Brown, M.D., F.A.C.S. Price, $15. Pp. 964, with 963 illustrations, 17 in color. Philadelphia: F. A. Davis Company, 1947.

Plastic surgery received a new impetus during and immediately after World War I; then came a settling-down period, which continued until World War II. Then, the enormous number of casualties and persons with maiming of various parts of the body brought an increasing number of plastic surgeons into the field of repair and reconstruction. This book is testimony to the amount of work now being done to make the lot of the *blessé* happier.

This volume will appeal to the general surgeon because it is based on a thorough understanding of surgical principles. These general principles make up Division I and illustrate free tissue grafting, shifting of tissue and transplantation. Wound healing, the care of burns and correction of scars receive special attention. Division II is concerned with the head and neck, especially with cosmetology and defects. Division III is confined to the trunk and considers procedures involving the female breasts, the genitalia and the sphincter ani and with the building of a new, extrathoracic, esophagus. The subjects considered in division IV are the hand and foot and the muscles, nerves and blood vessels which supply these members. The bones and joints are, of course, objective factors in any attempt to repair the limbs. In division V are cited about 126 cases. Black and white photographs illustrate the condition before and after the prosthesis is fitted. There are an index of illustrations and an index of subjects covering the entire book. At the end of each chapter is a complete bibliography. This is an excellent reference book, but it may be recommended for general reading also, since the style is interesting and the material comprehensive.

Histology and Histopathology of the Eye and Its Adnexa. By I. G. Sommers, M.D. Price, $12. Pp. 784. New York: Grune & Stratton, Inc., 1949.

Since a good textbook on ocular pathology has long been needed, a new work on the subject is a matter of considerable interest. Unfortunately, while the book does mark an advance, it leaves something to be desired.

The normal histology and general pathology of the eye are discussed in two short sections. The third section forms the body of the book and covers ocular

histopathology. Each chapter is followed by an extensive list of readings from the source material and by a most comprehensive bibliography, which gives evidence of tireless scholarship.

There is much valuable information to be found in the book, but it is not always expressed in a manner easily grasped by the novice. The illustrations are not as numerous as the subject requires and have, in general, a lack of distinctness which impairs their usefulness.

Aside from making use of this book for the readings, the bibliographies and the convenience of a single small volume, the average student may still turn to the sections on pathology incorporated in the volumes of Duke-Elder's "Text-Book of Ophthalmology."

Surgery of the Eye. Second edition. By Meyer Wiener, M.D. Price, $12. Pp. 426. New York: Grune & Stratton, Inc., 1949.

This highly readable and eminently practical book does not cover every surgical procedure in ophthalmology, but it does give those which the author has used successfully and can recommend. A single method, and in some instances several methods, are described for each condition requiring ophthalmic surgery.

The exacting requirements for a book presenting surgical technics are handsomely met by numerous, excellent illustrations and by clear, detailed exposition. This achievement is in the tradition of Meller. In addition, the book is noteworthy for its many and ingenious suggestions.

To the material in the first edition, published in 1939, are added descriptions of goniotomy for congenital glaucoma; implantation in evisceration, with preservation of the cornea, and corneal transplantation, in which the Wiener punch is used to obtain mechanically a beveled edge. It would have been interesting to have had more detailed description of the postoperative care, particularly in the matter of corneal transplantation, in which such care is so important but its omission does not detract from the general excellence of the book.

Directory of Otolaryngologic Societies *

INTERNATIONAL

Fourth International Congress of Otolaryngology

President: Dr. V. E. Negus, London, England.
General Secretaries: Dr. F. C. W. Capps and Dr. W. A. Mill, 45 Lincoln's Inn Fields, London, W. C. 2.
Place: London. Time: July 18-23, 1949.

Second Pan-American Congress of Oto-Rhino-Laryngology and Bronchoesophagology

President: Prof. Justo Alonso.
Secretary: Dr. Chevalier L. Jackson, 255 S. 17th St., Philadelphia 3.
Place: Montevideo. Time: January 1950.

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. William H. Johnston, 1515 State St., Santa Barbara, Calif.
Secretary: Dr. J. Milton Robb, 1553 Woodward Ave., Detroit 26, Mich.

American Academy of Ophthalmology and Otolaryngology

President: Dr. J. Mackenzie Brown, 1136 W. 6th St., Los Angeles 14.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100-1st Ave. Bldg., Rochester, Minn.

American Broncho-Esophagological Association

President: Dr. LeRoy A. Schall, 243 Charles St., Boston.
Secretary: Dr. Edwin N. Broyles, 1100 N. Charles St., Baltimore 1.
Place: Hotel Mark Hopkins, San Francisco. Time: May 25-27, 1950.

American Laryngological Association

President: Dr. Ralph A. Fenton, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Louis H. Clerf, 1530 Locust St., Philadelphia 2.
Place: Hotel Mark Hopkins, San Francisco. Time: May 23-24, 1950.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Robert C. Martin, 384 Post St., San Francisco.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y.

SECTIONS:

Eastern.—Chairman: Dr. Robert L. Moorhead, 125 Remsen St., Brooklyn.
Southern.—Chairman: Dr. William D. Stimson, 899 Madison Ave., Memphis, Tenn.
Middle.—Chairman: Dr. J. Marion Sutherland, 3001 W. Grand Blvd., Detroit.
Western.—Chairman: Dr. J. B. Naftzger, 6777 Hollywood Blvd., Hollywood, Calif.

American Otological Society

President: Dr. Philip E. Meltzer, 20 Charlesgate, W., Boston.
Secretary: Dr. Gordon D. Hoople, 1100 E. Genesee St., Syracuse 3, N. Y.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Inc.

President: Dr. Samuel F. Kelley, 47 E. 61st St., New York 21.
Secretary: Dr. Norman N. Smith, 291 Whitney Ave., New Haven 11, Conn.

American Society of Ophthalmologic and Otolaryngologic Allergy

President: Dr. Rea E. Ashley, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Joseph Hampsey, 806 May Bldg., Pittsburgh 22.

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.

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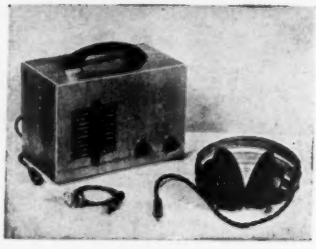

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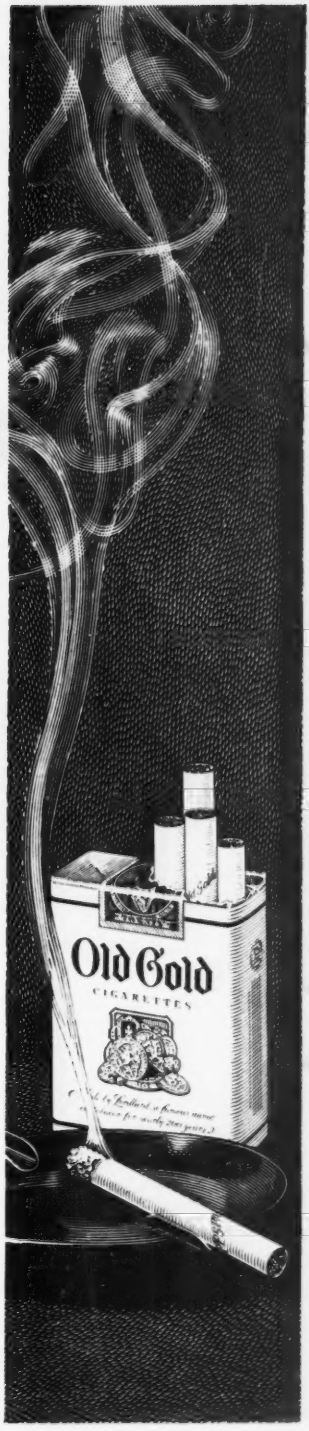

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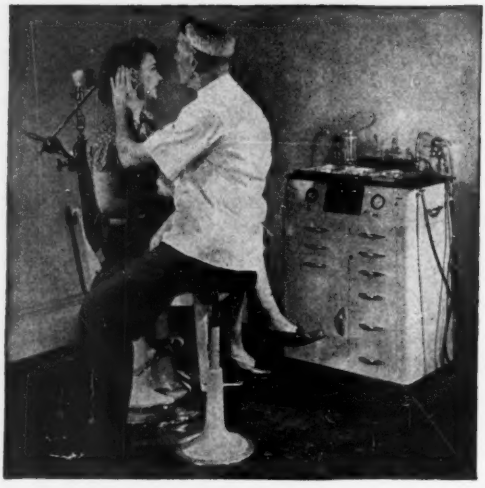

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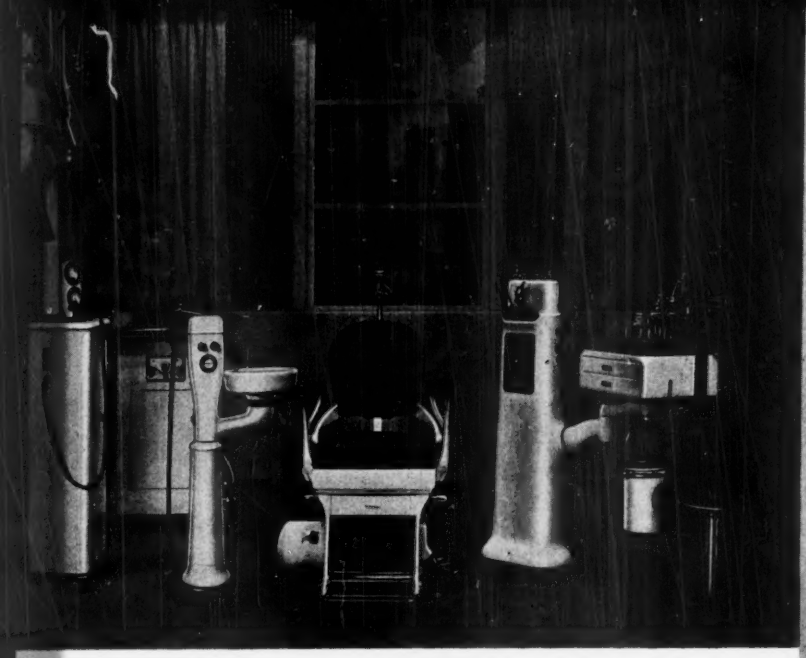

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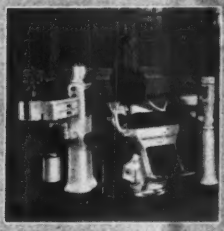

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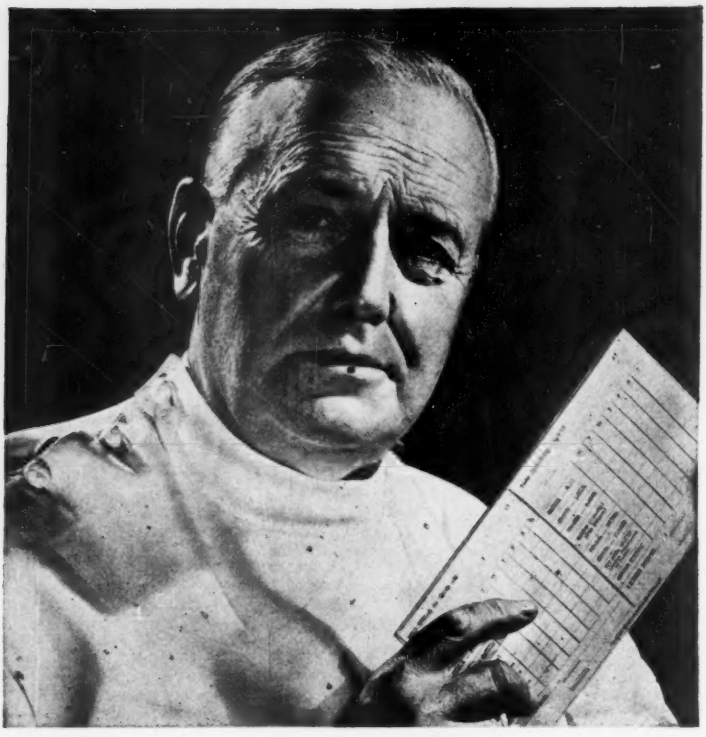

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